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ARCHIVES OF SURGERY

VOLUME 15

JULY, 1927

NUMBER 1

ACUTE AND CHRONIC PANCREATITIS

CLINICAL OBSERVATIONS

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PART I

The diagnosis of many pancreatic conditions is so difficult that a large proportion of the cases reported in the literature were definitely diagnosed only at operation or autopsy. Hence it is certain that the incidence of these conditions is probably far greater than has been generally recognized. The difficulty in diagnosis is largely due to three facts: 1. The pancreas is so deeply situated that it is usually inaccessible to palpation. 2. It is impossible to obtain a secretion from it in a state sufficiently pure for purposes of examination. 3. These diseases are often associated with other disorders of the digestive tract the symptoms of which are so prominent that they mask those produced by the pancreatic lesion.

It is our purpose in this communication to report briefly some of the cases of acute and chronic pancreatitis which have come under our observation. The following were cases of acute pancreatitis:

CASE 1—Acute pancreatitis in a diabetic patient with gallstones and acute nephritis. Drainage of gallbladder followed by death within a few hours.

M. M., a woman, aged 67, was admitted to the Hebrew Hospital on April 22, 1917. She had suffered from a mild type of diabetes for a number of years, but otherwise had had exceptionally good health. The acute illness was of less than twenty-four hours' duration. She was suddenly attacked with pain in the umbilical region, which traveled in the direction of the gallbladder and down toward the appendix. For six hours before admission there had been almost continuous vomiting of coffee-ground-like material. The bowels had been constipated for some time.

When first examined the patient was in a state of shock. The temperature was subnormal, the pulse was rapid, and the extremities were cold. The abdomen was distended, and there was marked rigidity with extreme tenderness.

in the epigastric area. The leukocyte count was 26,000. The urine contained albumin, a few red cells and many hyaline and granular casts.

The diagnosis of intestinal obstruction was made, although the possibility of acute pancreatitis was considered. An operation was performed at once. The abdomen was opened through a right rectus incision, and about a quart of free wine-colored fluid was found in the abdominal cavity. The gallbladder appeared distended, and the adipose tissue was covered with small white dots. These measured 1 mm or a little more in diameter, and were perfectly flat. At first they looked much like miliary tubercles, but on closer observation were recognized as areas of fat necrosis. In the region of the pancreas and the gallbladder there was considerable subperitoneal edema. We were undoubtedly dealing with acute pancreatitis. The gallbladder was drained, it contained a moderate amount of dark bile and a few small stones, hardly more than 1 mm in diameter.

Following the operation the patient continued in a state of shock, and the outlook appeared most unfavorable. She rallied again, however, but relapsed and died in a few hours.

CASE 2—*Acute pancreatitis, gallstones, drainage of gallbladder. Recovery*

J. B. E., a woman, aged 24, was admitted to the Church Home and Infirmary on March 31, 1919, complaining of intense abdominal pain. She had enjoyed good health and normal digestion until nine months before, when she had become pregnant. On various occasions during this period she had been seized with acute abdominal pain, located under the right costal arch and extending toward the right shoulder-blade. She had not had chills or fever, but on at least one occasion the attack had been followed by jaundice. There was constant tenderness under the right costal arch. In addition the patient was frequently troubled with eructations of gas and pain in the epigastrium which were relieved by the use of soda. A diagnosis of cholelithiasis had been made. The patient had gone through a normal confinement two weeks prior to entering the hospital, and during the two or three days before had had several attacks of pain in the region of the gallbladder, associated with fever. Hypodermic injections of morphine had been necessary. Later the pain radiated from the midepigastrium to the left side and the back, and considerable quantities of a yellowish fluid had been vomited, there was obstinate constipation. On examination, the patient appeared to be in a state of shock. The pulse was rapid, the temperature was subnormal and the extremities were somewhat cold. The abdomen was slightly distended. There was rigidity and extreme tenderness over the entire epigastric area. The urine contained a slight trace of sugar, albumin and acetone, and microscopic examination showed leukocytes, red blood cells and epithelial cells.

A diagnosis of cholelithiasis with possible perforation was made, and immediate operation was advised. A right rectus incision was made, and a yellow serous fluid was at once encountered. Milky patches of fat necrosis were noted in the omentum and peritoneum. These varied from 1 to 3 mm in diameter, and were evidently caused by acute pancreatitis. There was marked subperitoneal edema, especially in the region of the pancreas. The gallbladder was free from adhesions. It was not enlarged, but contained about thirty to forty, small mulberry-like stones, varying from 1 to 2 mm in diameter. The bile was ink, black and thick. The mucosa of the gallbladder was red, vascular and granular. A few of the small stones passed into the gallbladder from the

cystic duct A rubber drainage tube was inserted into the gallbladder, and three cigaret drains were placed around it The patient made a satisfactory recovery, and was discharged well on April 17, 1919

CASE 3—*Acute pancreatitis in a patient with cholelithiasis Drainage of gallbladder Recovery*

E R, a woman, aged 60, was admitted to the Church Home and Infirmary on April 9, 1925 She had always been in good health except for attacks of indigestion following meals, which had occurred at irregular intervals for some years They were characterized by the presence of pain, gas, eructations, and occasionally nausea and vomiting The attacks were of short duration, there were marked constipation and melena or clay-colored stools jaundice was absent

On the evening of April 7, 1925, the patient was suddenly seized with violent epigastric pain, nausea and vomiting necessitating the use of morphine There was intense pain in the epigastrium above the umbilicus and under the left costal arch, associated with intense nausea and frequent vomiting of a biliary secretion

When she was admitted to the hospital two days later, she looked ill and was in a state of shock, the extremities were somewhat cold, the pulse was rapid, and she was extremely thirsty She appeared to be in great pain, and was unable to sit up or turn over

Deep inspiration caused pain in the upper right quadrant The abdomen moved but slightly in inspiration, the walls, however, were not rigid There was tenderness under the right costal arch and in the epigastrium There was a leukocytosis of 22,700 The urine was normal except for a trace of albumin

The conclusion was that we were dealing either with an acute cholecystitis associated with a possible acute pancreatitis, or perhaps with a perforating peptic ulcer

The abdomen was opened through a McBurney incision A turbid fluid containing small flakes escaped when the peritoneum was incised The appendix was removed and proved to be two and a half times its normal size and enlarged toward the tip An upper right incision was then made, and the gallbladder was exposed It was tense and slightly adherent As the omentum between the stomach and transverse colon was drawn up, a white spot, about 1 mm in diameter, was noted, and when more of the omentum was exposed it was found to contain many small areas of fat necrosis With the brilliant yellow fat and striking white patches, the picture of fat necrosis, pathognomonic of an acute pancreatitis, appeared definite The gallbladder was drained and several small stones, together with a conglomerate calculus 1.5 cm in diameter, were removed A rubber drainage tube was inserted into the gallbladder, and two cigaret drains laid beneath it Marked subperitoneal edema was noted around the pancreatic region The pelvis was drained through the appendix incision The operation was followed by severe nausea and vomiting for a few days, and the incisions were slow in healing The patient was discharged, however, on May 10, 1925, in good condition

CASE 4—*Acute pancreatitis with gallstones and subsequent abscess formation Recovery*

V B, a woman, aged 34 first consulted us on Feb. 18, 1925 She had had good health until three months before but since then had complained of gnawing pains of a mild type in the upper part of the abdomen occurring at irregular intervals For the past month she had been seized once or twice weekly with

violent pains under the costal arch radiating into the right side of the back and frequently toward the right shoulder-blade. These attacks were of about two hours' duration, and necessitated the use of morphine hypodermically. During the attacks there was much distention and gaseous eructation. Fever and jaundice were not noted.

On examination the edge of the liver was palpable, but tenderness could not be elicited. The urine was normal, the gastric contents following an Ewald

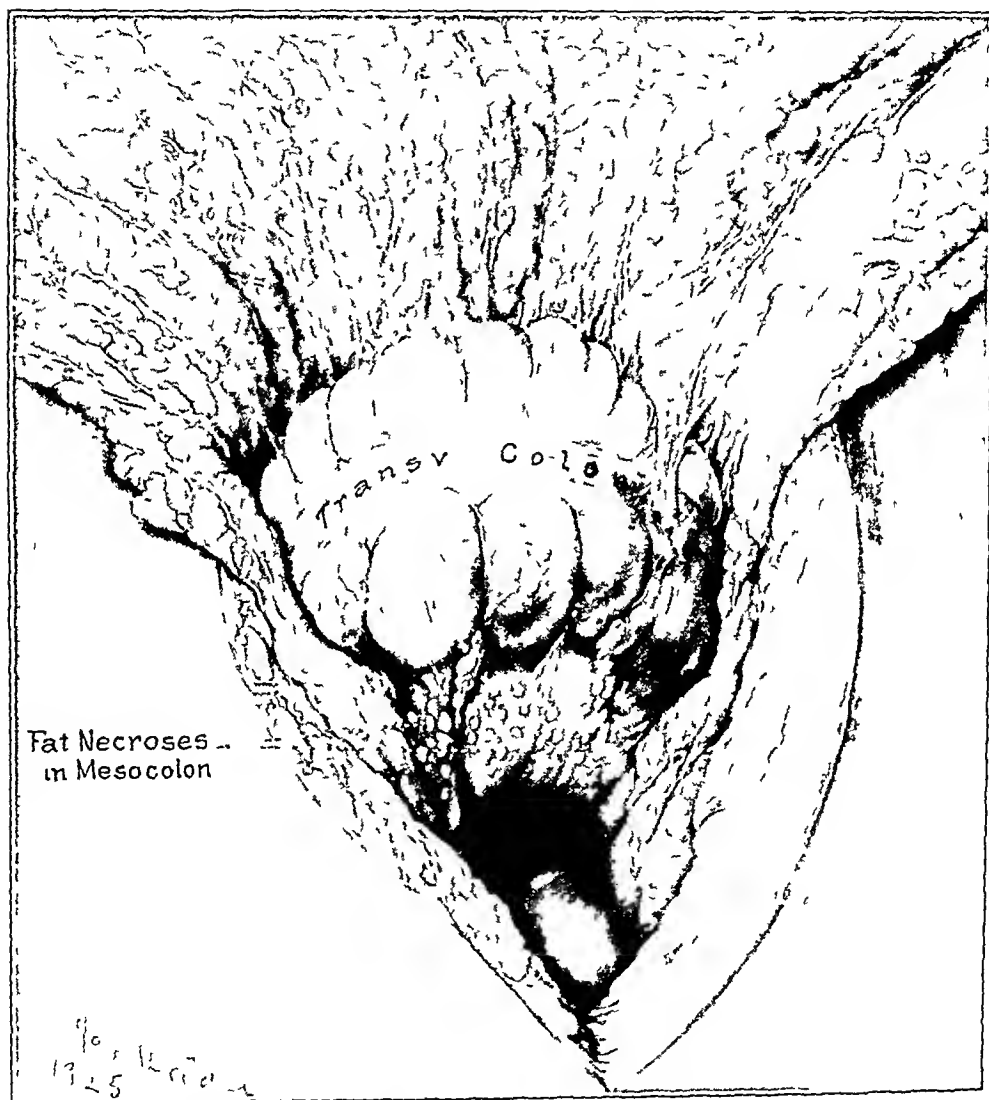


Fig 1—Fat necroses in the omentum

test breakfast showed total acidity 26, free hydrochloric acid, 19. A gastrointestinal roentgen-ray series showed adhesions in the upper right quadrant but no radiable stones. Cholecystitis with possible cholelithiasis was diagnosed.

The patient continued to have occasional attacks of a similar type until Sept 18, 1926. After that time she had three severe attacks of pain. During the last attack a new feature developed, in that the pain, which had previously

been localized, became general and was accompanied by tenderness over the entire abdomen

The patient was admitted to the Johns Hopkins Hospital on Sept 25, 1925. Examination revealed normal temperature, pulse rate, 78, hemoglobin 78 per cent, leukocytes, 15,480. She complained of considerable generalized abdominal pain and discomfort. She was slightly jaundiced, and there was an extreme tenderness over the gallbladder region, and generalized sensitiveness over the entire abdomen. Muscle spasm or rigidity was not present nor was there evidence of free fluid in the abdomen. The urine contained bile, but was otherwise normal.

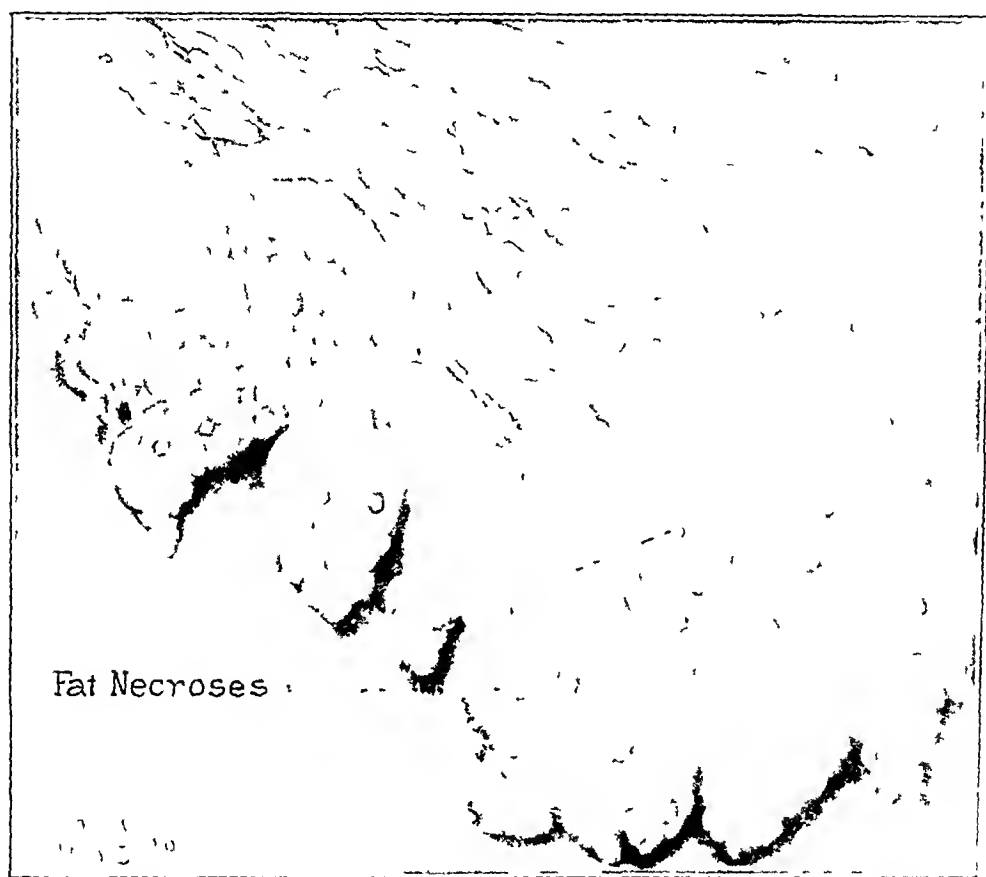


Fig 2—Fat necroses in the mesentery of the transverse colon

A diagnosis of cholelithiasis with possible acute pancreatitis was made. When the abdomen was opened, small, flat whitish yellow areas about 1 mm in diameter or smaller, were found scattered over the surface of the omentum (fig 1). In the omentum between the stomach and transverse colon there was an area, about 2 cm in diameter, sharply circumscribed somewhat puerled and containing myriads of these little areas of fat necrosis. The omentum and transverse colon were then pulled up and where the mesocolon lay over it a greatly enlarged pancreas could be detected. The organ was fully four times its natural size, and the fat presented numerous small areas of necrosis (fig 2). There were also stringy grayish blue areas in the fat suggesting that abscesses

might be developing. Adhesions did not appear between the peritoneum of the mesocolon and that adjacent to it.

The gallbladder was incised, and three stones, each about 1 cm in diameter, were removed. The stones were composed of smaller ones which had fused. There were also a number of small stones. Examination of the cystic and common ducts failed to reveal any further calculi. The gallbladder was drained with a rubber tube, three drains were placed around it, and another was carried down in the foramen of Winslow. Following the operation the patient was in a state of extreme shock, and the outlook was not particularly good.

Cultures taken from the gallbladder and peritoneal cavity were all negative. After operation, the temperature was normal, the incision healed *per primam*. The gallbladder tube was removed on the fourteenth day. The patient's appetite was very poor during the first two weeks, and during the third week she vomited continuously. The temperature began to rise, and during the third week it went as high as 101.5 F. She lost ground, could not retain any food, became weak and drained bile profusely through the fistula. On the twenty-first day a definite mass, occupying the lower third of the gallbladder incision, could be palpated. This mass appeared to be about 9 cm in diameter.

On Oct 19, 1925, a small incision was made over the lower third of the previous one, and induration in the fat was encountered. The indurated area was carefully penetrated with Kelly forceps, and fetid pus was found at once. After this had been carefully wiped off, long strings of what appeared to be disintegrated fat were removed. Some of these strings were fully 3 cm long and 1 cm broad. The wall of the abscess cavity was carefully palpated, and seemed to be intact at every point. The cavity was loosely packed with plain gauze. From the pus *B. coli* was grown in pure culture. The patient returned to the ward in splendid condition, and her convalescence from that time was uninterrupted. The drains were removed by the seventh day, and the temperature became normal on the eighth day. The bile escaping from the gallbladder fistula decreased just as soon as the abdominal abscess was opened. The fistula closed completely on the seventh day after the second operation.

The patient lost 18 pounds (8.2 Kg) during her stay in the hospital. When she left she had a splendid color, a good appetite, and was feeling well. The abscess incision was closing rapidly, but had not completely healed. She was discharged from the hospital on Nov 1, 1925. Microscopic examination of the necrotic tissue removed revealed that it consisted largely of necrotic fat.

ACUTE PANCREATITIS

Acute pancreatitis, according to the classical publication of Fitz,¹ occurs in three forms: hemorrhagic, gangrenous and suppurative. These three really represent various stages of the same process, which starts as an acute hemorrhagic lesion. It was Fitz, too, who first pointed out the clinical importance of fat necrosis and its relation to hemorrhagic and

¹ Fitz. New York M Rec 1 197, 225 and 253, 1889, Boston M & S J 127 571, 1892.

gangrenous pancreatitis, although this condition had been previously alluded to by Balser² and by Chiari³

In establishing the etiology of the hemorrhagic variety, it has been a question, according to Oser,⁴ whether the hemorrhage is primary and the inflammatory condition secondary or vice versa. According to Opie,⁵ inflammation is not present at the onset, and he therefore prefers the term hemorrhagic necrosis to that of hemorrhagic pancreatitis.

The gangrenous form is a later stage of the hemorrhagic lesion, while the suppurative variety is characterized by the formation of single or multiple abscesses.

ACUTE HEMORRHAGIC PANCREATITIS

This condition has also been termed pancreatic hemorrhage or acute hemorrhagic necrosis of the pancreas, for in it hemorrhage has been noted as a primary manifestation, followed subsequently by an inflammatory process. As we have already pointed out, in those instances in which hemorrhage and inflammatory changes are both present, it is usually impossible to decide which is the primary condition.

Opie⁶ has pointed out that the passage of bile into the pancreatic duct produced by gallstones in the diverticulum of Vater is a cause of hemorrhagic necrosis, and Archibald⁷ has shown that in addition, an infection of the bile is necessary in order to bring about this result. In most of the instances reported cholelithiasis was observed. According to Egdahl,⁸ in 42 per cent of these cases calculi are present either in the diverticulum of Vater or at the duodenal orifice of the pancreatic duct, and Opie considers this percentage too low. Gallstones were present in all four cases in our series.

Eggers⁹ maintains, from a study of his own cases, that infection is of minor importance as a causative factor in acute pancreatitis, but that the condition is brought about by the action of liberated pancreatic ferments on the surrounding tissues, in addition to some inflammatory condition associated with the gallbladder.

On the other hand, Ballantine¹⁰ considers that trauma plays an important rôle, and that common duct obstruction as well as infections

2 Balser. *Virchows Arch f path Anat* 90 520 1882

3 Chiari. *Prag med Wchnschr* 30 285, 1883

4 Oser, in *Nothnagel Diseases of the Pancreas*, Philadelphia W. B. Saunders Company, 1903, p 117

5 Opie, in *Osler Modern Medicine*, ed 3, Philadelphia, Lea & Febiger, 1926, vol 3, p 669

6 Opie. *Bull Johns Hopkins Hosp* 19 182 1901

7 Archibald. *Surg Gynec Obst* 28 529 (June) 1919

8 Egdahl. *J Exper Med* 9 385, 1907

9 Eggers. *Ann Surg* 80 193, 1924

10 Ballantine. *J Oklahoma M A* 27 264, 1924

diseases predispose to this condition. Cases in which trauma was noted as a cause of acute hemorrhagic necrosis, for instance, from a blow on the abdomen, have been reported by Selberg¹¹ and others.

Hofer¹² is of the opinion that, while biliary disease plays a most important rôle in the etiology of acute pancreatitis, inflammation can also be transmitted through the lymphatics, and that the changes occurring in the pancreas are attributable to the presence of trypsin-infected bile or duodenal contents. Marked inflammatory disturbances of the duodenum, with a consequent ascending infection, have also been thought responsible for this condition.

McCrae¹³ says that cases of acute pancreatitis have been observed at autopsies after death from infectious diseases. He believes that in these cases attacks of acute pancreatitis are present, but are so mild that they are frequently not recognized—a fact that would suggest a probable etiology by a hematogenous route.

Acute hemorrhagic pancreatitis occurs most frequently in men, although the four patients of our series were all women, the ages ranging between 24 and 67. The autopsy observations vary according to the duration of the lesion. The omentum and mesentery, retroperitoneal fat and abdominal peritoneum present a large number of yellowish white areas of fat necrosis varying in size from that of a pea to that of a dime. There is also often free blood-stained fluid in the lesser peritoneal cavity. It is not unusual to find gallstones and dark grumous bile in the gallbladder and occasionally gallstones may be palpated in the common duct or in the ampulla of Vater. The pancreas is usually enlarged and firm, dark, or mottled and friable. Many areas of fat necrosis are observed on the surface. The hemorrhagic necrosis spreads deeply downward, involving areas of both parenchyma and interstitial tissue, but leaving intermediate spaces of normal tissue. The cells of the parenchyma involved are in a state of necrosis with complete loss of nuclei. The necrosis also implicates the blood vessels of the pancreas, and produces hemorrhages of a more or less marked degree. Colon bacilli and streptococci are the usual organisms present.

Symptoms—Acute hemorrhagic pancreatitis frequently occurs in persons who have suffered from previous attacks of indigestion or biliary colic with or without jaundice. In these attacks, in addition to the pain, which may be of the biliary colic type or suggest gastric or duodenal ulcer, in some instances there is also nausea and vomiting. Ordinarily the attack begins with a sudden and violent pain, which is referred to the epigastrium and in some instances extends to the back or

11 Selberg. *Berl Klin* 38 923, 1901.

12 Hofer. *Arch f klin Chir* 131 313, 1924.

13 McCrae. *Atlantic M J* 28 555, 1925.

loms It may occur in intermittent paroxysms, but is usually constant In acute cases it may continue until death, which may occur even within a few hours The pain may be so violent as to suggest rupture of a peptic ulcer or of the gallbladder Collapse is common, with the usual symptoms of shock, a rapid, faint pulse, low blood pressure and cold extremities Nausea, vomiting and hiccups are early manifestations, and constipation is usually so obstinate as to suggest an acute intestinal obstruction In other instances diarrhea is an early symptom and ordinarily follows constipation, if this condition has previously been present In rare instances jaundice occurs Fever is rarely noted, though a leukocytosis is common, and glycosuria is occasionally found In a case reported by Rodriguez,¹⁴ an acute pancreatitis was associated with glycosuria and the patient died in a diabetic coma Dunn¹⁵ observed two cases in which diabetes followed as a sequel In case 1 of our series, the patient had a mild diabetes, and was suddenly taken with violent pain in the umbilical region, which was accompanied by continuous vomiting and signs of shock The constipation was so obstinate that a diagnosis of intestinal obstruction was made

In case 2 there had been definite evidence of former biliary colic with jaundice Pain was extreme in the epigastrium and radiated toward the left side Vomiting and marked constipation were present

In case 3 the patient had had indigestion for years It culminated in a sudden attack of violent epigastric pain, which radiated toward the left side and was followed by nausea, vomiting and shock

In case 4 there was a definite history of gallstone colic followed by an attack of general abdominal pain and jaundice

Examination in these cases reveals extreme tenderness in the epigastrium above the umbilicus, not only in the midline, but spreading across the abdomen to both sides In the early stages there is an absence of rigidity in this area, but soon this sign becomes marked An indistinct resistance may often be noted at first in this region, on deep palpation but as a rule, a tumor mass is rarely palpable until after three or four days Slate-colored patches are often observed on the abdomen and limbs, a condition which is associated with lividity of the face These are certainly rare in other acute abdominal disturbances

In cases 1 and 2 of our series there was extreme tenderness and rigidity in the epigastrium, while in case 3 there was tenderness under the right costal arch and also in the epigastrium In case 4 there was marked tenderness over the gallbladder region with a general sensitiveness over the entire abdomen

¹⁴ Rodriguez, Juan Acute Pancreatitis with Fat Necrosis Complicated by Diabetic Coma, *J A M A* 82 203 (Jan 19) 1924

¹⁵ Dunn *Lancet* 1 595 (March 20) 1926

Death may occur within a few hours or days, but if the patient survives for a period of a week or two, the stage of gangrenous pancreatitis ordinarily supervenes

In addition to the fulminating types of acute hemorrhagic pancreatitis, there are milder forms in which recovery occasionally takes place. Instances of this form have been reported by Waring and Griffiths¹⁶. Pain of any marked degree was observed in only about half of their cases. Brocq¹⁷ also points out that hemorrhagic pancreatitis is sometimes a mild condition in which pain is more or less diffuse, and is most severe at the end of digestion

ACUTE GANGRENOUS PANCREATITIS

This condition usually follows the hemorrhagic form, in which the symptoms manifested have been of a milder or subacute type. The pancreas presents a soft, friable appearance, and is darkish with yellowish areas of necrosis, which may be extensive. The lesser peritoneal cavity may be partly filled with necrotic, sanguineous, putrid contents. There is an extensive fat necrosis present around the pancreas and in the lesser peritoneal cavity, in which infections are caused by various forms of micro-organisms. General peritonitis is rarely produced, as the adhesions prevent the escape of infected fluid into the peritoneal cavity. Histologically, the boundaries between the acini of the pancreas become indistinct, and are replaced by granular detritus intermingled with red blood cells, the walls of the capillaries undergoing fatty degeneration.

Symptoms—If death does not occur as a result of the hemorrhagic stage, manifestations of gangrenous pancreatitis supervene. The fulminating symptoms now subside. The pain, tenderness and vomiting lessen, and the constipation is relieved. Recurrences of a milder type, however, are not infrequent.

The onset is characterized by fever and the formation of a mass in the epigastrium within a week or two after the beginning of the hemorrhagic stage. It may begin with a chill, or chills may occur during the course of the fever. The temperature is usually irregular, ranging from 100 to 103 F or higher. Only rarely is fever absent, a leukocytosis is the rule. The tumor in the epigastrium is ordinarily fairly definite, though it may vary in size, at times extending as far to the left as the spleen. At this stage the stools become soft, not infrequently diarrheic, and jaundice may occur. Glycosuria is unusual, though cases of diabetes following this condition after several months have been reported.

¹⁶ Waring and Griffiths. *Brit J Surg* **11** 476, 1924

¹⁷ Brocq. *J de chir* **25** 7, 1925

ACUTE SUPPURATIVE PANCREATITIS

Acute suppurative pancreatitis frequently follows hemorrhagic or gangrenous pancreatitis. In this form bacterial invasion is common so that suppuration with abscess formation is frequent. In some instances acute suppurative pancreatitis occurs as a primary infection. The purulent inflammation may extend to the lesser peritoneal cavity and produce peripancreatic abscesses. The infection may occur as a result of extension from adjacent organs through the blood stream, but it most commonly originates in the ducts. Many cases are caused by obstruction of the duct of Wirsung, due to the presence of gallstones in the diverticulum of Vater. In some instances a suppurative cholangitis has been noted as a causative factor.

Small multiple abscesses are present throughout the entire pancreas or are limited to certain areas. Large foci are produced by the coalescence of small abscesses, and as a result parts of the gland are destroyed.

Symptoms—The nature of the onset depends largely on its cause, that is, whether the condition is a result of an antecedent acute hemorrhagic or gangrenous pancreatitis or is due to carcinoma or suppurative inflammation of the bile passages. In most instances acute suppurative pancreatitis comes on suddenly, following an attack of indigestion or biliary colic, with severe epigastric pain which may radiate throughout the abdomen. There is epigastric tenderness. Nausea and vomiting are early manifestations. Fever of an irregular type is present, and chills are not uncommon. Constipation is usual and at times is followed by attacks of colliquative diarrhea. Abscesses occasionally rupture into the intestine, and blood and pus are discharged in the stools. Jaundice is common, and leukocytosis is often observed. Glycosuria is rarely noted.

In some instances the symptoms are of a milder type, the onset being less stormy and the pain less intense. In such cases there is often more discomfort without fever but with anorexia and weakness. The pains and fever gradually subside, and the disease may then pursue a more or less chronic course with periods of exacerbation.

Physical examination shows that the liver and spleen are enlarged, the epigastrium is distended, and in a certain proportion of instances a tumor mass or definite resistance can be felt on palpation. Case 4 of our series represents our only case of acute suppurative pancreatitis. The patient, three weeks after an operation for acute hemorrhagic pancreatitis, began to manifest signs of the suppurative form. The appetite became poor, and she began to vomit continuously. Her temperature rose to 101.5 F, and bile drained profusely from the fistula. The abscess was then detected.

The extension of the inflammation brings a complication of acute suppurative pancreatitis.

the encysted form, and is limited to the lesser peritoneum, though in some instances general peritonitis develops

Diagnosis—The sudden and fulminating onset of pain in the epigastrium accompanied by symptoms of shock points directly to the presence of acute hemorrhagic pancreatitis. The principal conditions from which it has to be differentiated are acute intestinal obstruction, especially if obstipation is present, cholelithiasis with rupture of the gallbladder, perforation of a peptic ulcer and mesenteric thrombosis.

When the transition from the hemorrhagic to the gangrenous type occurs, the epigastrium becomes distended, and a tumor mass becomes palpable in the epigastrium. Chills and fever are the rule.

As suppurative pancreatitis frequently follows the hemorrhagic and gangrenous forms, the history may sometimes furnish important information to help in the diagnosis. When a mass in the region of the pancreas occurs with chills and fever, suppuration must be suspected. If an abscess of this type ruptures into the intestine, the character of the stool serves as an aid in diagnosis. It is usually impossible to differentiate between the gangrenous and suppurative types.

The laboratory examinations are of distinct aid at times in the diagnosis of acute pancreatitis. The presence of glycosuria is especially valuable, and Musser¹⁸ has pointed out the importance of a high sugar content in the blood in these cases.

Course and Prognosis—In the fulminating types with hemorrhage, death frequently occurs within a few hours or days. Many surgeons, among them Moynihan,¹⁹ Vogel²⁰ and Ansperger,²¹ advise operation as a routine. On the other hand, the operative risk in the acute cases is so great that, if possible, according to our own experience, it is best to delay surgical intervention until the shock has somewhat subsided. When the disease has progressed to the gangrenous and suppurative stages, operation is indicated, but in these cases it often fails to save the patient, owing to the extent of the lesion and the multiple abscesses which have formed. However, whenever a large single accumulation of pus within the pancreas can be evacuated by incision and drainage, recovery may be expected.

Treatment—As has already been pointed out, except in rare instances little can be hoped for from surgical measures in the acute fulminating types of hemorrhagic pancreatitis. For immediate relief in allaying the violent pain and lessening shock, morphine in adequate doses is indicated, sometimes inhalations of chloroform may be utilized.

18 Musser. New Orleans M & S J **78** 10 (April) 1926

19 Moynihan. Ann Surg **81** 132, 1925

20 Vogel. Deutsche Ztschr f Chir **185** 71, 1924

21 Ansperger. Deutsche Ztschr f Chir **189** 189, 1924

Vomiting may often be controlled by means of gastric lavage and by the avoidance of food by mouth. The strength is best maintained with glucose by proctoclysis, and in addition normal salt and soda solution. Subcutaneous and intravenous injection of normal salt or glucose solution should be employed.

Statistics supplied by Gessner²² indicate that operations performed during this stage are more often fatal than during the later stages; that is, in the gangrenous and suppurative types. According to his data of forty-one cases of this disease in which an operation was resorted to during the first two weeks, recovery occurred in but one case (Halsted's), whereas of the twenty patients operated on during the later stages six recovered. Mayo-Robson and Cammidge²³ attribute the high mortality from early operation in acute cases to the fact that in many of these fatal cases intestinal obstruction had been suspected, and that these patients, already in a state of shock, were subjected to a prolonged search for the suspected lesion. Of fifty-nine of their patients operated on during the acute stage, twenty-three recovered (39 per cent).

Operation, however, is always indicated during the gangrenous and suppurative stages, and should be performed without delay. As has already been indicated, if the abscess is single and localized recovery may be expected as a result of effective drainage.

When operation has been decided on, an upper median abdominal incision should be made, and, as advised by Moynihan¹⁴ the pancreas should be approached through the gastrophatic omentum, gastocolic omentum, or in rare instances through the transverse mesocolon after reflection of the omentum. The pancreas should be cautiously isolated, packs being utilized with meticulous care in order to prevent the escape of the toxic pancreatic fluid into the peritoneal cavity. Evacuation of pancreatic fluid (if large quantities are present) is accomplished by aspiration, followed by incision into the pancreatic capsule and superficially into the gland itself to release fluid, blood and pus. Finally thorough drainage should be obtained by means of gauze surrounding a drainage tube passing through the anterior abdominal wall. Posterior drainage, in addition, is sometimes necessary. If the condition of the patient admits, gallstones, if present, should be removed.

The discovery of fat necroses at operation confirms the diagnosis. According to Mayo-Robson and Cammidge of six patients operated on for abscess of the pancreas recovery occurred in five (80 per cent) although in one instance relief was afforded only for a few weeks and in another but for a few months.

22 Gessner. *Deutsche Ztschr. f. Chir.* 54: 65, 1899-1900.

23 Mayo-Robson and Cammidge. *The Pancreas: Its Surgery and Pathology*. Philadelphia: W. B. Saunders Company, 1907, pp. 404, 407 and 433.

PART II

CHRONIC PANCREATITIS

For the reasons already given, the incidence of pancreatitis is far higher than is generally recognized. However, as a result of more careful study of the clinical manifestations, together with the results obtained through the laboratory observations, especially from the examination of the duodenal contents for pancreatic ferments, the diagnosis can now be made in many cases which heretofore would have been detected only at operation or autopsy.

Brief abstracts of the histories of fifteen cases of chronic pancreatitis studies are given below.

CASE 1—*Indefinite but urgent abdominal signs. Unusual twisting of the duodenum, chronic pancreatitis.*

Mrs. D. H. T., aged 40, for eight months had had marked indigestion, pain and a feeling of pressure after meals, nausea and occasional vomiting. She had had frequent diarrhea, had lost much flesh and complained of extreme weakness. On March 12, 1903, she was suddenly seized with violent abdominal pain which was followed by intense shock. When she was first seen, her appearance strongly suggested an abdominal perforation. There was a definite board-like rigidity over the entire right side of the abdomen. The patient had a subnormal temperature and rapid pulse and was extremely ill. Further examination could not be made. An exploratory incision at the Cambridge Hospital revealed a twisted and somewhat thickened duodenum. The pancreas was much enlarged and extremely hard and thickened. Fat necrosis, however, was not noted. The duodenum was straightened out as far as possible. The patient, although in a state of extreme shock during the entire operation, soon improved and made a rapid recovery.

The pancreas, though presenting the typical appearance of a chronic inflammatory condition, could hardly have accounted for the acute symptoms, which were in all probability produced by a sudden twist in the duodenum.

CASE 2—*Chronic pancreatitis with symptoms suggesting cholelithiasis or cancer.*

J. C. D., aged 35, first consulted us on March 27, 1903. For the preceding five or six years the patient had had digestive disturbances, being unable to eat certain articles of food. He was easily nauseated by disagreeable sights and odors, and for fourteen years he had had occasional attacks of abdominal colic.

About August, 1902, he began to suffer pains in the right lumbar and hypochondriac regions. These were not constant and were varied in severity, at times they were sharp and lancinating, at other times dull and aching. The patient had complained of indigestion, which had been more or less acute during this period. These attacks were characterized by severe nausea and frequent vomiting which would appear suddenly, most frequently at night, accompanied by severe pains in the epigastrium. The vomited material consisted mainly of undigested food particles and mucus, occasionally it contained blood. There was often a gushing of saliva into the mouth. After the severe pain disappeared, a soreness would still remain over the abdomen. The fulminating pains and attacks of vomiting which occurred only occasionally at first, became more frequent, so that he had attacks every three or four days. The

bowel movements were diarrheic, and occasionally contained blood, especially after a severe attack. The patient had lost 40 pounds (18.1 Kg) in weight.

On examination he was found to be emaciated. The mucous membranes were pale, his face was much drawn, his tongue slightly coated, the pulse was weak, the radial arteries were slightly thickened, and the heart and lungs were normal.

The abdomen was somewhat distended, the surface presented a distinct cyanotic appearance, and the capillaries were markedly distended. There was tenderness in the epigastrium and beneath the right costal arch. The gastric contents after an Ewald test breakfast showed total acidity, 40, free hydrochloric acid, 0, much mucus. The urine was normal. A blood count showed red blood cells, 5,168,000, leukocytes, 5,625, hemoglobin 50 per cent. Otherwise the patient was normal. At first the case was considered one of cholelithiasis, on the other hand, the rapid emaciation, together with the absence of free hydrochloric acid in the gastric contents, pointed in a measure to carcinoma of the stomach, notwithstanding the absence of palpable tumor. The diagnosis appeared so doubtful that the patient was kept under close observation for a while.

Numerous examinations of the gastric contents revealed conditions similar to those described. The paroxysmal attacks of pain became more frequent and intense. The pain was almost entirely in the epigastric region, which was now constantly tender to pressure. The stools were copious, of a mushy consistency, had a cadaverous odor, were extremely fatty and contained blood. Fat globules, fatty acid needles and fragments of striated muscle were abundant.

From a consideration of the nature of the stools, the paroxysmal pains in the epigastrium and the rapid emaciation, a diagnosis of chronic pancreatitis was made.

At operation on June 1, 1923 (performed by the late Dr. John W. Chambers) the liver was found normal, calculi were not detected either in the gallbladder or ducts. The stomach was fastened by adhesions to the under surface of the liver near the gallbladder, it did not contain masses. The pancreas was hard, firm and tense, giving a sensation as of scar tissue, at one point the pancreatic tissue was so hard that the presence of a calculus was suspected, which, however, was not found on closer investigation. The head of the pancreas was much enlarged. There was a definite chronic pancreatitis. Cholecystostomy was performed, and the patient made an uneventful recovery, gaining 42 pounds (19.1 Kg) within a few months. When last seen (September, 1908), he was in good health.

CASE 3—*Chronic pancreatitis with adhesions between the stomach and liver*

Z. S., a man, aged 64, was admitted to the Church Home and Infirmary, on June 30, 1905, complaining of indigestion. The patient had suffered for the preceding year and a half with nausea, occasional vomiting, pressure and fullness following meals and pain in the epigastrium. The condition occurred irregularly, and was not dependent on the ingestion of food. Constipation was usually present and was often followed by attacks of diarrhea with copious stools. There was a great loss of weight and great weakness.

On physical examination, the patient appeared much emaciated. The heart and lungs were found to be normal. The abdomen was soft, enlargements or masses could not be detected. Analysis of the gastric contents after an Ewald test breakfast showed a total acidity of 45, free hydrochloric acid 10. His urine was normal. The stools were large and soft, they contained much undigested fat and muscle fibers. The blood count showed red blood cell

5,096,000, leukocytes, 5,600, hemoglobin, 70 per cent, the differential count was normal

From the age of the patient, his loss of flesh and the digestive disturbance, we concluded that we were probably dealing with carcinoma of the stomach, and an exploratory operation was determined on

At operation adhesions were noticed between the stomach and liver, and the head of the pancreas was found hard and firm, presenting definite indications of a chronic pancreatitis. The adhesions were released, the gallbladder was drained, and the patient made a good recovery

CASE 4—*Chronic pancreatitis with gallstones and chronic appendicitis*

S C, a woman, aged 41, was admitted to the Church Home on April 22, 1908, with a history of having suffered during the preceding three years from acute attacks of abdominal pain, located under the right costal arch and radiating toward the right shoulder-blade. These occurred at irregular intervals, were frequently accompanied by chills and fever, and were occasionally followed by jaundice. During the last eight months, there had been much indigestion in the form of pressure and fulness following meals and not infrequently nausea and vomiting. The patient had lost 20 pounds (9 Kg) in weight and complained greatly of weakness and of obstinate constipation.

On examination the heart and lungs were found normal. The abdomen was soft, the edge of the liver was palpable and tender to pressure.

Analysis of the gastric contents following an Ewald test breakfast revealed a total acidity of 22, free hydrochloric acid, 0. The urine was normal. The stools were large and bulky, they contained much undigested fat and muscle fibers. Examination of the blood did not present abnormalities.

The diagnosis of cholelithiasis with possible chronic pancreatitis was made, and an exploratory operation was advised. At operation the gallbladder was found enlarged and thickened. It contained from forty to fifty hard, dark, slightly faceted stones, these were removed, and the gallbladder was drained after removal of the appendix, which was considerably dilated and adherent throughout its length. The pancreas was much enlarged, firm and markedly indurated, it presented every evidence of being chronically inflamed.

CASE 5—*Chronic pancreatitis in a woman with a duodenal ulcer firmly adherent to the head of the pancreas*

A B, a woman, aged 46, was admitted to the Church Home and Infirmary on May 22, 1913, with a history of indigestion extending over a period of at least six years. At first she had had much pain several hours after meals, which was usually relieved by the ingestion of food and by the use of alkalis. The appetite at times was good, but the patient was afraid to eat. A carefully regulated diet was then prescribed. The pain gradually disappeared, and distention began to manifest itself in the region of the stomach, during the past two years there had been nausea and vomiting. The latter was apparently of the retention type, and occurred at intervals of three or four days. During the past year, there had been obstinate constipation, alternating with diarrhea and the passage of copious stools.

When first seen, the patient appeared extremely weak and emaciated, and because of the distress due to the digestive disturbance she insisted on an operation.

Physical examination showed that the organs of the chest were normal. The abdomen was extremely relaxed. Tender areas or masses could not be made out,

but the stomach appeared prolapsed, and there were occasional evidences of peristaltic waves

On exploration the stomach was found dilated and prolapsed, the lower border lying in the pelvis. The transverse colon was also greatly prolapsed. A definite duodenal ulcer with constriction was found in this region, and the duodenum was firmly adherent to the pancreas. The head of the pancreas was hard and firm, and there was every evidence that we were dealing with a chronic inflammatory process especially involving this portion of the organ.

A posterior gastro-enterostomy was performed, and then a Coffey operation in which the tissues between the stomach and transverse colon were brought together with ten black stitches, which were then fastened to the anterior abdominal wall. At the completion of the operation the stomach was in good position. The patient stood the procedure well, and made a satisfactory recovery.

CASE 6—Chronic pancreatitis with adhesions in the region of duodenum and gallbladder. Acute suppurative cholangitis and cholecystitis

F J S, a woman, aged 63, was admitted to the Church Home and Infirmary on April 15, 1914. Her general health had always been good, though she had had obstinate constipation for years. Her illness began in April, 1913, with diarrhea which lasted for the entire summer, during which she lost 80 pounds (36.3 Kg.) in weight. In December, 1913, she had a sudden attack of acute pain in the upper right side of the abdomen, which radiated to the upper right side of the back and shoulder-blade. This was accompanied by nausea and vomiting and the pain was so intense as to require a hypodermic injection of morphine. The attack was followed by jaundice, and the patient was forced to remain in bed for three weeks. Following this the slightest indiscretion in diet induced similar attacks, so that recurrences occurred every two or three weeks. On examination the patient presented evidence of great loss of weight, the thoracic organs were normal. The abdomen was flabby, the edge of the liver palpable and tender to pressure, and an indefinite mass was felt in the epigastrium.

An examination of the urine showed the presence of albumin, acetone, bile and granular casts. The examination of the blood showed red blood cells, 4,100,000, white blood cells, 6,250, hemoglobin, 60 per cent, the differential count was normal.

From the history of marked loss of weight, the apparent attacks of cholelithiasis and the indefinite nodule in the epigastrium the probable diagnosis of carcinoma of the stomach and liver together with cholelithiasis was arrived at and operation was advised.

On the following day a right rectus incision was made and the stomach was found adherent over a mass just above the lesser curvature. There were recent adhesions in the region of the duodenum extending over the gallbladder. The gallbladder was thick and shrivelled. There was not any evidence of a mass in the stomach itself. The mass above the lesser curvature of the stomach was continuous with an enlarged and nodulated pancreas and on further investigation appeared to form a part of it. The liver was much larger than normal, extending as far down as the umbilicus, it was free from any growth. It was evident that we were dealing with a chronic pancreatitis. The gallbladder was drained. It contained a small amount of pus, but did not contain bile or stone. The drain was passed down toward the lesser curvature of the stomach and lay beneath the gallbladder. The patient seemed to do well for the first two or four hours and then began to lose ground. She secreted only a small amount of urine, bronchopneumonia developed and she died on April 17, 1914.

At autopsy the pancreas was found enlarged, measuring 13 cm from head to tail. It was hard and firm, section showed that the lobulation was rather coarse, and there was an increased amount of gray translucent interlobular connective tissue. Areas of necrosis were not noted in the fat about the pancreas. The ducts were patent and contained much sero-sanguineous fluid. Additional evidences of an acute suppurative cholangitis and a subacute nephritis were present.

CASE 7—Marked case of chronic pancreatitis with enlargement of the liver in a patient affected with pulmonary tuberculosis

W S, a woman, aged 59, consulted us on May 25, 1916, for indigestion which had been present for about ten or twelve years, but which had recently become greatly aggravated. She complained of a sense of fulness and distention after meals with occasional nausea. There had never been any violent attacks of pain in the abdomen, though there was almost constant discomfort. Diarrhea was of frequent occurrence, the stools often being copious and of an oily, greasy appearance. In addition, the patient had complained for a long time of cough and expectoration, and occasionally of fever, night sweats and extreme weakness.

On examination the lungs presented evidence of marked consolidation of both apexes, the heart was normal. The abdomen was distended, the edge of the liver was palpable and tender to pressure.

Analysis of the gastric contents following an Ewald test breakfast showed a total acidity of 28, free hydrochloric acid, 0. The stools were liquid, of a foul odor and contained large amounts of undigested fat and muscle fibers. The duodenal contents showed an absence of the trypsin ferment and a diminution in amount of the amyllopsin and steapsin.

Roentgen-ray examination revealed a marked tuberculous consolidation of the apexes of both lungs. The gastro-intestinal series pointed to adhesions in the upper right quadrant.

The diagnosis of possible disease of the gallbladder with chronic pancreatitis was made, and an exploratory operation was advised.

At operation, the pancreas was found to be about three times its normal size and extremely hard. The edge of the liver near the gallbladder presented a puckered appearance as if from an old inflammation. The gallbladder was free from adhesions, but on account of the chronic inflammatory condition of the pancreas, it was drained. The tuberculous process did not appear in the abdomen. The patient stood the operation well and made a satisfactory recovery.

CASE 8—Chronic pancreatitis with a history of cholelithiasis followed by symptoms of indigestion, loss of weight and strength

B W, aged 58, first consulted us on Sept 5, 1916, for indigestion which had persisted for the preceding six years. He first had a sudden attack of acute abdominal pain located under the right costal arch and radiating toward the shoulder-blade on the same side. These attacks were accompanied by chilly sensations which were followed by fever. Several such attacks had occurred during the preceding few years. In addition to these attacks, there was more or less continuous abdominal distress, flatulence, pressure and fulness following meals, constipation alternating with diarrhea and great loss in weight, 35 pounds (15.9 Kg), and strength.

On examination the patient was found to be poorly nourished and markedly emaciated. The mucous membranes were pale, the tongue was coated, the pulse weak and the blood pressure was, systolic, 110 diastolic, 55. The heart and lungs were normal. The abdomen was somewhat distended, the liver

slightly enlarged, masses were not noted on palpation and tenderness was not evident. Analysis of the gastric contents following an Ewald test breakfast showed achylia, total acidity, 25, free hydrochloric acid, 0. The urine was usually normal, but occasionally contained traces of sugar. The blood count showed red blood corpuscles, 4,168,000, white blood corpuscles, 6560, hemoglobin, 54 per cent, otherwise normal. Results of the Wassermann test were negative.

The stools were usually copious and frequent, from eight to ten a day. At times they were solid, but usually they were liquid, light and foul and contained much undigested fat and muscle fibers. Examination of the duodenal contents for ferments revealed that amylase was present, steapsin was absent and that there was only a trace of trypsin. Results of a roentgen-ray examination were negative.

The diagnosis of chronic pancreatitis was based on a history of attacks caused by gallstones and indigestion, the nature of the stools, the occasional traces of sugar in the urine, the result of the analysis of the pancreatic secretion and the loss of weight and strength.

The patient lived for four years, during which there were periods of from one to two months of relief followed by serious recurrences of the symptoms noted above. Finally he succumbed following an exhausting diarrhea.

CASE 9—Chronic pancreatitis in a patient with cholelithiasis. Pancreas nodular and twice its normal size.

H. L., a woman, aged 48, was admitted to the Church Home and Infirmary on May 17, 1919. For the preceding five or six years, she had had indigestion in the form of pressure and fulness after meals and marked distention, occasional nausea and vomiting occurred. During the year before, there had been a number of acute attacks of abdominal pain, beginning beneath the right costal arch and radiating toward the right side of the back and shoulder-blade. The pain was so intense as to require hypodermic injections of morphine for relief. These attacks were accompanied by chills and fever, as well as nausea and vomiting, and were followed by jaundice. In the three months before she came to the hospital the condition had materially changed. During this period epigastric pain had been almost constant, though severe at times and slight at others, it had radiated to the left side and was associated with frequent nausea, vomiting and extreme weakness. The patient had lost 30 pounds (13.6 Kg.) and was slightly jaundiced. On examination the organs of the chest were found normal. The abdomen was soft and there was a marked tender area in the midepigastrium extending toward the left side. A definitely tender area was also noted in the right lower quadrant with muscle spasm in this region.

The urine was normal except for a trace of bile. The diagnosis of cholelithiasis with chronic appendicitis was made and operation was advised. On May 19, 1919, a McBurney incision was first made, and the appendix was removed. It was found thickened near its tip, and the cecum was bound down by old adhesions.

A right rectus incision was then made and a marked thickening and enlargement of the pancreas was noted. It was nearly twice its natural size and extremely nodular. In the gallbladder there was a composite stone composed of a number of small ones that had been fused. It reminded one of a piece of broken concrete. Further stones were not observed and there was no thickening of the walls of the gallbladder. The gallbladder was drained. The pan-

made an uneventful recovery, and was discharged on June 13, 1919, in good condition

CASE 10—Chronic pancreatitis with gallbladder adhesions and enlarged lymph glands along the common duct

G M H, a woman, aged 18, admitted to the Church Home and Infirmary, on May 16, 1922, had formerly been in excellent health with a good appetite and without indigestion, constipation had, however, been present since childhood Her illness began during the later part of January, 1922, with nausea and gradually increasing jaundice The stools were copious, extremely constipated and of an ashy gray She did not have any pain Following this attack, the duration of which was about two weeks, the jaundice cleared up, and the patient was apparently in good health until March 15, 1922, when she had the "grip," which lasted over a period of two weeks Following this she again became jaundiced, and remained so

On physical examination, the heart and lungs were found normal The abdomen was symmetrical, the liver was palpable just beneath the costal arch and was firm and tender Other tender areas were not noted

The urine was normal, except that it contained much bile The stools were large, slate-colored, and contained much undigested fat and muscle fibers

From the long-continued and painless jaundice, together with the bulky stools containing undigested fat and muscle fibers, the diagnosis of chronic pancreatitis was considered

The patient was given several preliminary intravenous injections of calcium chloride and was operated on, May 27, 1922

A right rectus incision was made, the gallbladder exposed and found to be small Numerous adhesions were noted between the gallbladder and duodenum and omentum These were liberated A chain of enlarged lymph glands was observed along the common duct, some of them 1 cm in length and 1 cm in breadth, and the pancreas was found much enlarged as well as hard and nodular The gallbladder was incised and drained with a small rubber tube and two cigaret drains placed beneath the gallbladder Evidence of gallstones was not present The patient made an uneventful recovery and was discharged from the hospital in good condition on June 21, 1922 She was still well on Nov 16, 1926

CASE 11—Chronic pancreatitis simulating carcinoma of the head of the pancreas Relief under medical treatment

S S, a man, aged 76, consulted us on Sept 10, 1923, for a digestive disturbance from which he had suffered for more than three months and prior to which he had always enjoyed good health He complained of diarrhea, discomfort in the epigastrium, occasional nausea, extreme weakness and a loss of 22 pounds (10 Kg) in weight The stools numbered about five a day and occurred mainly in the morning They were extremely bulky, oily, soft and fetid

On physical examination the patient presented the appearance of having lost considerable flesh, he was somewhat anemic, and the conjunctivae showed a slight icteric tint His thoracic organs were normal, his blood pressure was systolic, 155, diastolic, 80

The abdomen was soft, the liver was slightly enlarged, and its surface was smooth, the spleen was not palpable Tender areas or masses were not noted

A gastro-intestinal roentgen-ray study did not reveal any defects in the stomach or duodenum The duodenum, however, was pulled over and held

firmly under the region of the liver by adhesions. Other abnormalities were not found.

The examination of the urine revealed a trace of bile, and sugar intermittently, but it was otherwise normal. The stools were soft and bulky and characteristically showed much undigested fat and muscle fibers. The blood count was as follows: red blood cells, 4,100,000, white blood cells 5,160, hemoglobin, 62 per cent, differential count, normal. The Wassermann reaction was negative.

A chemical test of the blood gave negative results with the exception of the blood sugar, which on several occasions reached 0.13 per cent in the fasting state while at other times it was normal.

It was impossible at first to determine whether we were dealing with a chronic pancreatitis or cancer of the head of the pancreas.

However, under a carefully regulated diet and rest, the stools became less frequent, and the patient gradually regained 15 pounds (6.8 Kg.) in weight. He still at times had recurrences of diarrhea with the characteristic stools and glycosuria, which extended over a period of five or six days to a week but which were always relieved by care in diet and rest. After more than three years since this patient manifested his first symptoms, he was in good condition. This must definitely exclude the presence of carcinoma.

CASE 12—Chronic pancreatitis with a history of indigestion and acute abdominal pain followed by jaundice, apparently from the gallbladder. Diarrhea, absence of pancreatic ferments. Improvement.

A R., a man, aged 69, was admitted to the hospital on Jan. 28, 1926, complaining of indigestion. During the previous few months he had had attacks of indigestion characterized by acute pain in the upper part of the abdomen radiating toward the right shoulder-blade and followed by jaundice. The attacks would appear at irregular intervals, were sufficiently severe to require hypodermic injections of morphine and were frequently accompanied by chills and fever. Recently there had been diarrhea with six or eight liquid stools a day. The patient had lost much strength and flesh.

On examination the skin and sclerae were found to be extremely jaundiced. The thoracic organs were normal. The abdomen was markedly distended and the liver enlarged. Tenderness was not felt. The urine was examined frequently and revealed the presence of sugar at intervals. Examination of the blood gave the following results: red cells, 4,200,000, white cells, 9,150, hemoglobin, 84 per cent, differential count, normal. Wassermann test normal, blood chemistry, normal. The roentgen-ray examination revealed adhesions in the upper right quadrant. The gastric analysis showed a total acidity of 20 and in absence of free hydrochloric acid, after an Ewald test breakfast. The stools were large, soft or liquid and contained much undigested fat as well as muscle fibers. An examination of the duodenal contents showed a total absence of the steapsin and trypsin ferments, amyllopsin was present in normal amount.

The patient was placed in bed and given a liquid and soft diet. The treatment consisted of daily nonsurgical biliary drainages according to the Ewald method. The pain gradually subsided, the jaundice disappeared, there was a gain in weight and his general condition became much improved. After three months, however, he continued at times to pass bulky, oily stools.

In chronic pancreatitis there is an increased production and thickening of the interstitial tissue of the pancreas with destruction of the glandular

substance. Ordinarily, the increase in connective tissue is primary and may be diffuse, involving the entire gland, or may be limited to certain areas. There are two well recognized types of this condition—the interlobular and the interacinar forms. In the first variety the interlobular connective tissue is greatly increased and thickened, and the glandular structures are compressed. In the second, diffuse areas or bands of connective tissue are formed which penetrate within the glandular acini and separate them, while the interlobular tissue is only slightly invaded.

According to Opie,²⁴ of thirty cases of chronic pancreatitis occurring at the Johns Hopkins Hospital, twenty-one represented the interlobular and nine the interacinar type.

The interlobular form occurs as a result of occlusion of the pancreatic duct or as a result of infection caused by calculi situated in the biliary or pancreatic passages, and is caused by such organisms as the colon bacillus, streptococci or occasionally the typhoid bacillus. As the disease progresses, fibrous tissue in large amount may be produced, the entire gland being converted into a narrow band of connective tissue surrounding a duct containing calculi. At this stage many lobules are destroyed, and the acini within become atrophied. The islands of Langerhans are less affected at this stage, but as the disease progresses, they are finally damaged by the pressure, and disturbances of the blood supply, and atrophy takes place.

In the acinar variety of chronic pancreatitis, the gland is less hard and nodular than in the interlobular form. There is a diffuse fibrosis between the acini, the interlobular tissue being but slightly involved. Even in its early stages, there is involvement of the islands of Langerhans. These are surrounded by connective tissue which separates them from surrounding structures, and within the islands bands of connective tissue and the increased fibrous proliferation bring about an atrophy of the cells of the island which finally leads to their destruction and replacement by connective tissue. In a considerable number of instances, there is a definite sclerosis of the arteries.

Chronic interacinar pancreatitis is usually a result of infection, and is produced by such conditions as cirrhosis of the liver, alcoholism and arteriosclerosis. Its etiology in some instances, according to Opie, is obscure. In chronic interlobular pancreatitis the infection is usually introduced through the duct of the gland, while in the interacinar form the infection is probably introduced through the blood supply.

In hemochromatosis, which is associated with chronic pancreatitis, the most prominent lesion is in the interacinar tissue and islands of Langerhans, in addition, there is an increase in the interlobular connective tissue.

²⁴ Opie in Osler. *Modern Medicine*, ed. 3. Philadelphia, Lea & Febiger, 1926, vol. 3, p. 686.

According to Opie,²⁴ of thirty cases of chronic pancreatitis observed at the Johns Hopkins Hospital, seventeen were noted in men and thirteen in women. The disease occurs largely between the ages of 40 and 60. In our series of fifteen cases there were eight men and seven women, the ages ranging between 18 and 76, the greatest number (twelve) occurring between 40 and 70.

The relation of cholelithiasis to chronic pancreatitis has been a matter of considerable interest, for chronic pancreatitis has not uncommonly been noted at operation for gallstones. Opie²⁴ considers that this relationship can exist, even though the pancreatic duct is not occluded with calculi. It is probable that in these cases the infection spreads from the biliary passages to the pancreatic duct or from the duodenum. Though infection through the lymphatics has been noted by Deaver and Sweet, Opie claims that definite proof of its occurrence has not yet been established.

It is interesting in this connection to note that Deaver and Pfeiffer²⁵ have demonstrated disease in the pancreas in 33 per cent of all cases of cholecystitis, and that chronic pancreatitis has frequently been observed as a secondary development following a cholecystectomy.

Symptoms—Until a comparatively few years ago, this condition was considered rare, as many cases escaped recognition, but with the greater precision in diagnosis, together with the aid afforded by newer laboratory procedures, many more cases should now be recognized. The diagnosis of chronic pancreatitis is frequently based on the firmness and hardness of the head of the pancreas noted on palpation at operation. In some instances, however, as has been pointed out by Pratt and verified by Deaver, this condition may be merely a temporary swelling due to congestion.

Although the symptoms are rarely definite, chronic pancreatitis should be suspected in a patient presenting a chronic dyspepsia with or without a history of biliary colic, if he complains, in addition, of a severe or slight epigastric pain situated often to the left of the midline and also referred to the left shoulder-blade, associated with nausea, vomiting, emaciation, extreme weakness, slight jaundice and occasionally with ptialism and stomatitis. Occasionally the pancreas may be palpated and may be tender to pressure.

In certain instances intermittent glycosuria, hyperglycemia, belly soft and fetid stools aid in arriving at the diagnosis. The stools in these cases number from four to eight daily, usually occur in the morning and

25 Deaver and Sweet: Prepancreatic and Peripancreatic Disease. A Consideration of Anatomic Basis of Infection from Gallbladder. *J. A. M. A.* **77**: 104 (Jan. 19) 1921.

26 Deaver and Pfeiffer: *Tr. Am. Surg. A.* **39**: 121, 1921.

contain undigested fat and undigested protein in the form of striated muscle fibers

It is interesting to note that in our series of fifteen cases of chronic pancreatitis, there was a history of chronic dyspepsia in eleven, biliary colic in five, epigastric pain in five, extreme loss of weight in nine; marked weakness in seven, jaundice in seven, ptysis in two, intermittent glycosuria in three, and diarrhea with fatty stools in twelve

Many of the symptoms are often lacking, and consequently the diagnosis becomes extremely difficult, as the condition does not have any characteristic pathognomonic symptom. In drawing conclusions, therefore, great stress must be placed on the history of gastro-intestinal disturbances occurring with slight jaundice, progressive loss of weight and strength and the appearance and nature of the stools

Great assistance in diagnosis may sometimes be derived from the examination of the duodenal contents for pancreatic ferments, for in chronic pancreatitis their activity is markedly diminished. By means of the method devised by McClure, Wetmore and Reynolds,²⁷ accurate studies of this secretion have been made in normal persons and in some affected with chronic pancreatitis. According to Silberman and Denis,²⁸ who used the same method, normal persons present an enzyme activity of lipase of from 0.8 to 2 mg, amylase, from 1.3 to 2.6 mg, protease, from 1.3 to 2.9 mg. In patients with chronic pancreatitis the following figures were noted: lipase, from 0.1 to 0.8 mg, amylase, from 0 to 0.8 mg, protease, from 0.2 to 1.6 mg.

Bassler²⁹ has worked out a quantitative test for pancreatic activity which is easily applied clinically. After much experimentation, he has concluded that the amylase is the most satisfactory ferment in testing for pancreatic activity. His method may be utilized with advantage for the detection of changes in the pancreatic secretion in cases of chronic pancreatitis. But although these methods of laboratory investigation may be extremely helpful in the diagnosis of chronic pancreatitis, the evidence afforded by the study of the duodenal contents must always be interpreted with caution.

Diagnosis—In the differential diagnosis, the following conditions must be considered: cancer of the head of the pancreas, cancer of the common bile duct, cancer of the liver and stones in the common duct.

²⁷ McClure, Wetmore and Reynolds. New Methods for Estimating Enzymatic Activities of Duodenal Contents of Normal Man, *Arch Int Med* **27** 706 (June) 1921, and *Am J M Sc* **167** 649, 1924.

²⁸ Silberman and Denis. *South M J* **17** 549, 1924.

²⁹ Bassler. Quantitative Test of Digesting Pancreatic Activity, Easily Applied Clinically, Tests for Volume of Pancreatic Juice and Bile Secretions, *Arch Int Med* **35** 162, 1925.

In cancer of the head of the pancreas, the onset is gradual without pain, and when jaundice manifests itself it remains constant and deepens. The feces are bulky, however, and contain large amounts of undigested fats. There is extreme and progressive loss of weight with anemia and finally edema of the extremities and ascites. The differential diagnosis is, however, extremely difficult in many instances and even at operation it is not unusual to arrive at the erroneous conclusion of cancer of the head of the pancreas when the condition is actually a chronic pancreatitis. At times when operating for gallstones, the surgeon discovers a large hard and often nodular mass in the region of the head of the pancreas which will lead to the diagnosis of cancer. A similar conclusion may be reached in certain instances in which there has been marked loss of flesh, jaundice without pain and with fatty stools. His diagnosis is frequently incorrect, though his treatment may be correct, the hard nodular mass may be due to a chronic pancreatitis, in which case drainage of the gallbladder will bring about recovery, or at least improvement.

The three following cases with similar histories illustrate this condition.

CASE 13—*Chronic pancreatitis with attacks of cholelithiasis*

L. M., a man, aged 52, gave a history of attacks of cholelithiasis extending over a period of three years. These attacks appeared irregularly, and were violent at times, although the patient enjoyed good health in the intervals. The last attack, which had occurred four weeks previously, was somewhat unlike the others. The pain was less violent and was located in the epigastrium. Chills and fever were present, and jaundice followed within a few days. The fever, however, gradually subsided but the jaundice continued. Constipation which was present at first gradually disappeared and was followed by diarrhea. The patient had lost about 20 pounds (9 Kg.) in weight. Physical examination at this time revealed a tenderness under the right costal arch but a mass could not be detected. A diagnosis of cholelithiasis with involvement of the common duct was made. At operation stones were found in the gallbladder and in the common duct. The head of the pancreas was much enlarged, hard and hard. The conclusion was reached that we were dealing with a cancer of the head of the pancreas with cholelithiasis. The stones were removed and the gallbladder was drained. The patient had a stormy convalescence from the operation and continued to lose weight. During the following weeks and of diarrhea occurred with profuse greasy stools in which much undigested was noted. After four weeks however these conditions subsided and there was gain in weight, the jaundice entirely disappeared and the patient continued in good health.

CASE 14—*History of indigestion, jaundice, extreme constipation, and weight diminution of pancreatic ferments. Diagnosis of cancer of pancreas.*

J. S., a man, aged 61, had always been in good health until the onset of illness. About three months before he came to the hospital he began to complain of indigestion, nausea, occasional vomiting and discomfort after meals. About four weeks before he was admitted to the hospital he began to

the onset of jaundice, which gradually became marked. Constipation had been obstinate, and he had lost 15 pounds (7 Kg) in weight.

Examination of the abdomen did not reveal tenderness, enlargement or masses. The gastric secretion at this period showed an absence of free hydrochloric acid, and the duodenal contents a diminution of its ferments (trypsin and amylase). An attempt to obtain bile by means of nonsurgical biliary drainage was unsuccessful. The diagnosis of carcinoma of the head of the pancreas was made. At exploratory operation the gallbladder was found apparently normal, and did not contain stones. There was a single stone in the common duct. The head of the pancreas was hard and nodular, and on palpation gave a distinct impression of carcinoma. The common duct stone was removed, and the duct and gallbladder were drained. The jaundice disappeared within a few weeks, and the patient made an uneventful recovery and has since been well.

CASE 15—*Chronic pancreatitis with indigestion followed by jaundice and diarrhea with large, fetid, fatty stools, loss of weight. Diagnosis: Cancer of the head of the pancreas.*

F. L., a man, aged 56, had enjoyed good health until five months previously. He then began to complain of indigestion in the form of pressure and fullness after meals, nausea and occasional vomiting. The indigestion had gradually increased, and within the last month the patient had been jaundiced. Since then there had been diarrhea with the passage of five or six large, fetid, fatty stools occurring mainly in the morning. He had lost 30 pounds (13.6 Kg) in weight.

On physical examination nothing abnormal could be detected in the abdomen. The diagnosis of probable carcinoma of the head of the pancreas was made. At exploratory operation evidence of stones in the gallbladder or duct could not be detected. The head of the pancreas was hard and firm. The gallbladder was drained, and the diagnosis of carcinoma of the head of the pancreas supposedly was confirmed. The patient, however, made an uninterrupted recovery. The jaundice disappeared, and he has since gained 45 pounds (20.4 Kg) in weight, and is in splendid health.

Cancer of the common duct is frequently accompanied by gallstones, and if the disease extends to the papilla, the symptoms may be much like those observed in chronic pancreatitis.

In cancer of the liver, the nodulated areas on the surface of this organ and its rapid enlargement aid in differentiating it from chronic pancreatitis.

The differential diagnosis from cholelithiasis is at times difficult, especially in instances of chronic pancreatitis that are associated with paroxysmal pain. While these attacks are similar to those noted in cholelithiasis, the pain is usually less intense. The tenderness is more likely to be situated in the epigastrium, and the pain radiates toward the left shoulder-blade. The stools do not present the great excess of fat in cholelithiasis usually noted in chronic pancreatitis. As chronic pancreatitis is so frequently associated with gallstone disease, the presence of typical symptoms of cholelithiasis may be of value as pointing to the necessity of early operation at which both conditions may be corrected.

Prognosis—The prognosis of chronic pancreatitis is ordinarily not unfavorable if the disease is recognized sufficiently early to forestall serious injury to the pancreas. The greater the destruction of the gland, the more unfavorable is the prognosis. In many instances the morbid progress of the disease is slow, and many months or years may elapse before definite signs of it are manifested. The causes of death from this condition are usually progressive loss of flesh and exhaustion, hemorrhage or diabetes.

Treatment—Robson and Cammidge²³ correctly point to the prophylactic treatment of this disease, especially by the early removal of gallstones before complications have been produced. Such conditions as duodenal catarrh and inflammation of the biliary passages should also be overcome by means of appropriate treatment. As preventive measures for these conditions, as well as for the treatment of the milder forms of chronic pancreatitis, the following procedure should be prescribed. The patient should be placed on a carefully regulated diet, with small meals at regular intervals not too far apart. Prolonged fasting should be avoided, for the process of eating increases the flow of bile and of pancreatic juice, and on this account it is well for the patient to take an additional light meal at night. Fats should be reduced to a minimum while, on the other hand, carbohydrates should be consumed in increased amounts. Too much meat should not be eaten and only the lean part should be used. Milk is permissible, and green vegetables and fresh fruits may be partaken of freely. Cereals and stale bread are also useful foods in this condition. Alcoholic stimulants must be forbidden while coffee and tea may be taken moderately, and tobacco should be avoided or the amount used greatly reduced. The drinking of large amounts of water, and the free use of alkaline mineral waters are indicated.

Since Rothchild and Rosenthal have shown that hypercholesterolemia exists in cases of cholelithiasis, it is well, in the management of cases of pancreatitis dependent on gallstone disease, to lessen the cholesterol content of the food as far as possible, both before and after operation. This can be accomplished by placing the patient on a fat-free diet. All foods rich in fats should be excluded, as butter, olive oil, cream and eggs.

In addition to keeping to his diet the patient should avoid overexertion, and should be given occasional purges of calomel or frequent alkaline salines.

Nonsurgical biliary drainage according to the Lyon method will do much, by avoiding or overcoming infection in the biliary tract, common and pancreatic duct, to prevent the onset of this serious disease. This method of treatment is especially applicable when there is no obstruction of these passages without the presence of stones. The impaired pancreatic function may be aided at times by the administration of pancreatic preparations. If after a thorough trial of the treatment outlined above

toms persist, surgical intervention must be considered, especially if gallstones are present, and there is persistent jaundice

In the surgical treatment of this disease, the cause should be eradicated as far as possible. If gallstones or pancreatic stones are present, they should be removed, if possible, and infection should be overcome. It is always important to secure adequate and effective drainage of the biliary and pancreatic passages by means of cholecystostomy, cholecystenterostomy or gastrocholecystostomy.

If the cause can be completely removed at an early stage, at least a clinical cure may be expected. Even in advanced cases, an arrest of the pathologic process may be hoped for, and the nonaffected portion of the pancreas may carry on the function of the gland, though perhaps to a lesser degree.

Inasmuch as it is difficult to overcome the infection entirely in all instances, even by surgical measures, occasional nonsurgical biliary drainages may be continued with advantage after operation in order to avoid recurrences.

SUMMARY

The incidence of both acute and chronic pancreatitis is far greater than has generally been recognized, and as the symptomatology of these conditions is usually indefinite, the correct diagnosis is too rarely made. In acute hemorrhagic pancreatitis the onset is ushered in by a sudden violent pain in the epigastrium, with signs of shock, which may suggest rupture of a peptic ulcer, gallbladder or even of the appendix. It may be followed by death within a few hours or days. The acute gangrenous form follows the hemorrhagic type, in which the symptoms manifested have been of a milder or subacute form. This condition manifests itself by the appearance of chills, fever and the formation of a mass in the epigastrium within a week or two after the onset of the hemorrhagic stage. The acute suppurative type, in which abscesses are formed, frequently ensues as a subsequent stage after either of the two types first named. It is associated with chills, fever and frequently with jaundice, nausea, vomiting and severe epigastric pain. Attention must be directed particularly to the significance of fat necrosis as an important accompaniment, especially of hemorrhagic and gangrenous pancreatitis, and its value as a diagnostic sign at operation. Owing to the great operative risk, the question as to whether immediate surgical intervention should be undertaken has not as yet been definitely established in cases of acute hemorrhagic pancreatitis. Many surgeons consider that it is best to delay until shock has somewhat subsided. Each case must be considered separately; a routine rule cannot be laid down. When the disease has progressed to the gangrenous and suppurative stages, speedy operation is indicated.

In the study of chronic pancreatitis, the relation of this condition to cholecystitis and cholelithiasis is a matter of considerable interest. Although the symptoms of chronic pancreatitis are rarely definitive, its presence should be suspected if, in a patient who has suffered from a chronic dyspepsia with or without a history of biliary colic there is present a severe or slight epigastric pain associated with nausea, vomiting, emaciation, extreme weakness, slight jaundice and occasionally with ptyalism and intermittent glycosuria. In many instances the bulky, soft, fetid and oily stools containing undigested fat and protein aid in arriving at the diagnosis. Great assistance may be rendered in diagnosis by an examination of the duodenal contents for pancreatic ferments which may be markedly diminished in their activity in this condition.

In the diagnosis difficulty may be experienced in differentiating between cancer of the pancreas and chronic pancreatitis. Even at operation, cancer of the pancreas is sometimes diagnosed when the condition is actually a chronic pancreatitis.

In the prophylactic treatment of this condition attention must be especially directed to the early removal of gallstones before complications have occurred and, as preventive measures, a carefully regulated diet should be followed, together with nonsurgical biliary drainages to avoid or to overcome infection in the biliary tract and prevent the onset or progress of this serious disorder. When the disease is definitely established, immediate operation is advised. If gallstones or pancreatic stones are present, they should be removed and infection overcome. It is important to secure effective drainage of the biliary passages by means of cholecystostomy, cholecystenterostomy or gastrocholecystostomy.

OSSIFYING FIBROMAS OF THE JAW

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The region of the jaw may be the site, not only of those peculiar tumors which are associated with the formation of the teeth, but also of most of the tumors which occur in other parts of the body. Of the latter group, the fibroma is probably the most frequent. In rare instances it has been observed to be associated with ossification and has been termed an osteofibroma. As a review of the literature has revealed only fourteen of these cases, it may be of value to point out some of the characteristics in connection with three cases which have come under my observation.

REPORT OF CASES

CASE 1—M D, an Italian girl, aged 12, entered the Children's Memorial Hospital on April 2, 1925, complaining of a lump on the right side of her jaw. The swelling had first been noticed about a year before and had grown steadily. It had never caused any pain or discomfort. Her family and past history was negative.

Physical Examination—She was a well built, healthy looking girl. On the outer side of her right jaw was a hemispherical mass about 1 inch (2.5 cm) in diameter. The mass was hard and firmly fixed to the ramus of the jaw near the angle. The surface of the mass was smooth and not tender to palpation. Blood examination showed 10,000 white blood cells. The Wassermann reaction was negative. Her pulse rate and temperature were normal. A series of roentgenograms of the jaw showed an area of increase bone penetration, circular in outline, in the anterior third of the right side of the jaw. This area was suggestive of a bone cyst.

Operation and Course—On April 3, 1925, under ether anesthesia an incision was made over the tumor from the inside of the mouth, in the mucous membrane at the base of the lip. The mucous membrane was stripped back, exposing the bony tumor. A chisel applied to this bone revealed a soft mass of tumor tissue lying in a bed of the jaw bone and covered by a thin layer of bone. A capsule was not seen, but the tumor was easily removed, leaving a clean base. The tumor tissue was cream colored, homogeneous and hyaline in appearance, and friable. It was not vascular but looked much like a sarcoma. The bed of the tumor, however, looked so smooth and the removal of the tumor, although not encapsulated, appeared to be so clean cut that further excision did not seem to be warranted. The bed of the tumor was cauterized with phenol and packed with iodoform gauze.

The wound healed, and the child was discharged from the hospital clinic three weeks after operation. Eleven months after operation she was again examined, and evidences of recurrence could not be seen on physical examination or in roentgenograms.

Pathologic Examination by Dr W Hibbs—Paraffin sections of the tumor tissue were stained with hematoxylin and eosin. All of the sections were essentially similar. About nine-tenths of the entire tissue consisted of densely ramifying well-stained strands of adult connective tissue fibers. These

strands generally were from 5 to 12 fibers thick, and their course ran in many directions. Blood vessels were scarce, and those present had clumps of small round cells adjacent to them.

At the distal portions of all sections, the entangling fibrous tissue strands intimately surrounded islands of new bone formation of various shapes. The shape of these varied from round clumps of from 3 to 5 cells to irregular trabeculae of bone from 2 to 3 cells thick, and from 15 to 20 cells long. Red blood cells infiltrated the tissue only in clumps adjacent to the islands of new bone formation. A capsule was not present (figs 1 and 2).

CASE 2—W. N., a white man, aged 66, entered the Presbyterian Hospital on Sept. 6, 1922. He said that forty-seven years previous to examination he had

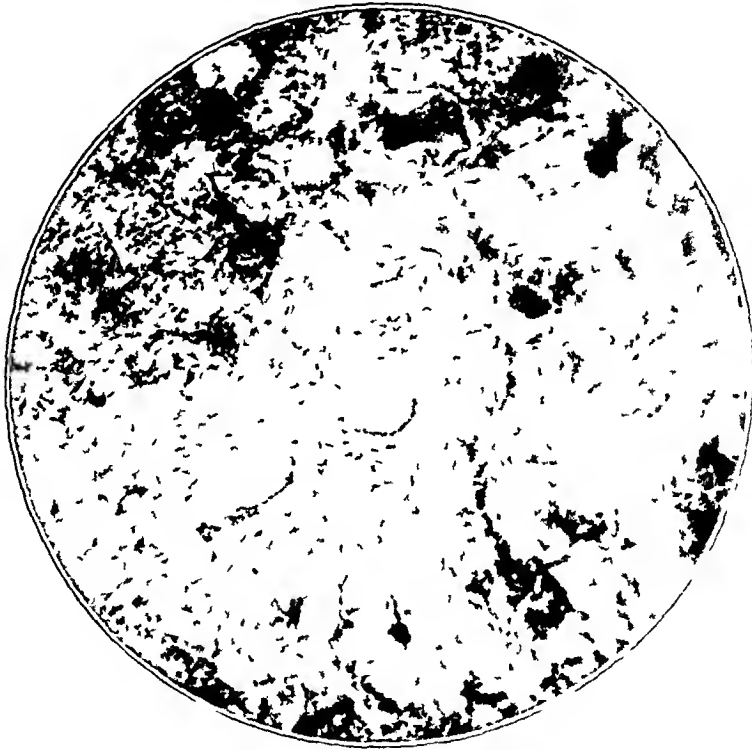


Fig. 1 (case 1)—Osteofibroma of the lower jaw—low power magnification.

had a swelling of the lower right cheek that discharged pus for a long time. It had finally healed and had not caused further trouble. Twelve years before the patient had noticed a nodule growing on the upper jaw just inside the gum of the teeth. The nodule was painless but grew rapidly. The mass was removed by a surgical operation and the patient did not have a very pleasant recovery about seven months before he was admitted to the hospital when he said that his 'jaw was swelling up'. Since then the swelling had increased in size but without pain. His general health had been good and he had gained weight.

Physical Examination—The patient was a well developed man with a swelling in the right jaw but apparently was not troubled with pain. In the right jaw there was a hard immovable mass in the gum between the teeth. The surface of this mass was somewhat elevated but not very prominent to palpation. The right upper polar teeth were loose.

teeth were in bad condition. Palpable glands were present in the left anterior triangle, and one could be felt on the right anterior triangle of the neck. There was a marked inguinal adenopathy on both sides. His temperature and pulse rate were normal. Results of the examinations of the urine and of the blood, including the Wassermann test, were negative.

Roentgenographic Examination—Evidences of the formation of new bone were present in the region of the right maxillary antrum, irregular in density and outline, forming a new growth that extended upward, involving the antrum, and downward into the mouth through the upper jaw. The growth extended almost to the floor of the orbit.

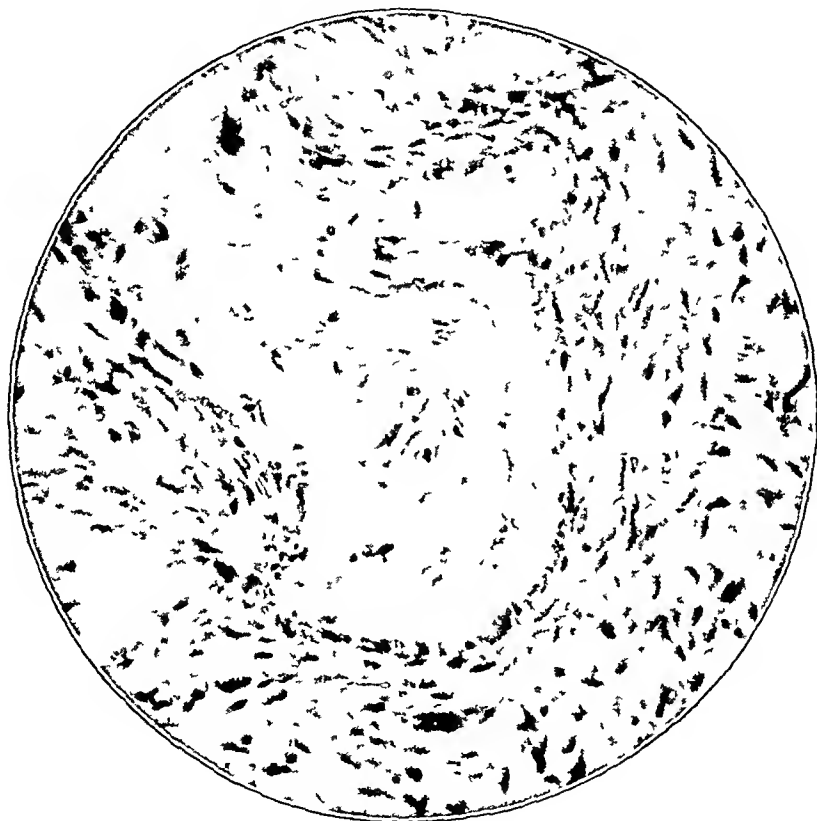


Fig 2 (case 1) —Osteofibroma of the lower jaw, high power magnification

Operation and Course—On Sept 9, 1922, this patient was operated on by Dr A D Bevan. Under ether anesthesia, the right external carotid artery was ligated above the site of the superior thyroid through a small incision in the side of the neck. The tumor was exposed by an incision, extending from the middle of the upper lip to the nasal septum, then laterally around the wing of the nose and upward along the side of the nose to a point about 2 cm from the lower edge of the orbit. From that point the incision extended outward, parallel to the orbital edge, to the external angle of the eye. The flap of soft parts marked out by the incision was dissected from the bone and reflected laterally. The maxillary bone, with the tumor mass, was separated from its attachments, and was removed, with the exception of the portion which formed the floor of the orbit. The space left by the removal of the tumor was packed with iodoform gauze, and the flap of soft parts was sutured back into place.

The wound healed, and two weeks after operation the patient was discharged from the hospital. The cavity into the mouth was clean and granulating. The patient had a complete postoperative paralysis of all the branches of the right facial nerve below the level of the orbit.

Pathologic Report (Dr. H. Oberhelman)—Microscopic examination showed that in one section of this tumor there was a network of delicate collagenic fibers of varying density. In places they assumed a whorllike arrangement. In this network there were elongated and many spindle-shaped deeply staining nuclei, which were densest where the collagenic fibers were most compact. In places two, three or even four of the elongated nuclei were grouped simultaneously in part, giant cells. There were also round cells, in places aggregated also where more diffuse. The entire section was relatively avascular, the lymphatic channels being more numerous than the blood vessels.

In another section there were skin and subcutaneous tissue along one side. The latter was dense, although in places it contained many fat spaces. The dense tissue was continuous with periosteum and this in turn gradually shaded into bone made up of trabeculae. These anastomosed variously and enclosed for the most part fat spaces, but many contained concentric layers of spindle-shaped cells and collagenic fibers, gradually shading into bone.

In another portion there was a collection of polymorphonuclear leukocytes, round cells and plasma cells in a background of many fibroblasts, which diminished peripherally and gradually merged into bone. In this place, in somewhat eccentrically placed, there was the root of a tooth surrounded by a dense connective tissue capsule.

CASE 3—T. S., an Italian laborer, aged 62, entered the Presbyterian Hospital on Jan. 2, 1917. He complained of a swelling in the upper jaw with inability to close the mouth tightly. The first symptom of this trouble was a severe pain in the pharynx, associated with swelling in the neck. This attack occurred eighteen years previous to his coming to the hospital and lasted for four days. It was not severe enough to confine him to bed or to require drugs for relief. One year later he had an attack of rheumatism in the right arm and leg, which lasted for thirteen months. A year after he recovered from this illness he noticed a small, red, painless, soft swelling about the size and shape of a lima bean behind the upper incisor tooth. This swelling had increased to the size of a pigeon's egg within four years, and he had had the mass removed at the County Hospital. Just previous to this operation all his teeth had been extracted. Four years before he came to the Presbyterian Hospital he had had a severe, uniform red swelling on the right side of his face, which had disappeared under hot applications after ten days. For the past two years he had been unable to bring his jaws together tightly, and had had a sharp pain in the left upper buccal region radiating over the entire left cheek. He had a growth in the cheek for twelve years, similar in type to the previous one, which was removed. The growth was not painful unless it was pressed on.

His general health had always been good except as noted above. During the past twelve years he had gained 10 pounds (4.5 kg.). He smoked a smoking pipe with strong tobacco and drank three or four glasses of beer daily. His history, otherwise, was negative.

Physical Examination—The patient was a well developed man without any abnormalities except in the region of the upper jaw. A swelling measured 5 cm. across, extended from the middle of the upper lip to the left. The surface of this mass was hard, smooth and shiny. It was not

pation, without any evidences of fluctuation. The mucosa over the entire mass was red, rough and irregular. The mass appeared to have a definite border, and could be readily outlined.

Operation and Course—On Jan 4, 1917, under ether anesthesia, an incision was made in the mucous membrane over the tumor mass, and most of the tumor was enucleated along the line of cleavage with a periosteotome. The remainder of the mass was curetted out, and an iodoform gauze pack was inserted.

The cavity healed rapidly under gauze packings, and the patient was discharged from the hospital on Jan 12, 1917, with a small discharging sinus. The wound healed completely in a short time, and has not recurred up to date.

Pathologic Report (Dr H. Oberhelman)—Microscopic examination of a typical section of the tumor of the superior maxilla showed many elongated pale-staining nuclei, others spindle-shaped and still others round. All were widely scattered in a moderately loose, network-like arrangement of collagenic fibers. In some places, these fibers were compact, and were arranged in wavy bundles, between which there was considerable extravasated blood in some areas. Along one side of the section, there were irregular islands of trabeculated bone. These islands lay in, and were closely associated with, the loosely arranged collagenic fibers, but in a few places tongue-like projections of these bony trabeculae were continuous with the more compact wavy bundles of connective tissue, gradually shading into the loosely arranged collagenic fibers. Bone marrow was absent from the spaces formed by the bony trabeculae, the spaces being occupied by the collagenic fibers. The tissue was relatively avascular. Some of the prominent blood vessels lay in the center of the loose tissue in the enclosed trabecular spaces.

In two or three places there were dense collections of small, deeply-staining nuclei, well demarcated from the surrounding tissue. These were not unlike giant cells. They also resembled small obliterated blood vessels. In one place these nuclei formed a column resembling a longitudinal section through such a blood vessel.

ABSTRACTS OF CASES FROM THE LITERATURE

CASES 4, 5, 6 AND 7 (Hildebrand, quoted by Hippel¹)—"In rare cases fibroma formation is combined with the osteoma. Then between the bony trabeculae are found strands of spindle cell fibrous tissue, and the impression is received that from the beginning the bony new formation was combined with the fibroma new formation, so regular are the bony formation and the fibroma formation in the entire tumor. Such cases I have observed four times on the upper jaw. The upper jaw formed an entirely solid mass without a maxillary cavity."

CASE 8 (Bellin, reported by Gagnier²)—A woman, aged 22, had had a swelling in the right cheek noticed at the age of 14. It was attributed to carious teeth. Almost all the teeth on the right side had been extracted, but the tumor continued to grow.

Physical Examination—The skin was normal and not edematous. There was a protuberance of the right zygomatic arch and the anterior surface of the entire right upper jaw, so that its normal depressions and elevations were smoothed out. Tender or soft spots were not felt on palpation. The hard palate on the right side bulged downward, most markedly toward the alveolar

1 Hildebrand, quoted by Hippel. *Lehrbuch der allgemeinen Chirurgie*, 1909, p. 345.

2 Gagnier. *These de Paris*, 1910.

process. The swelling was of an even, bony hardness throughout. The alveolar process was widened and of the same hardness.

Transillumination from the mouth outward gave total darkness on the right side. The left side was normal. The examination was otherwise negative. The diagnosis was a benign tumor.

Operation—A partial resection was made. A window was opened into the canine fossa. Directly beneath the cortex was a spongy tissue. The operator removed this tissue piece by piece to a depth of 2 cm. without finding a line of demarcation between it and healthy tissue. Tumor tissue was removed as far down as the periosteum of the hard palate, upward as far as the floor of the orbit. A maxillary cavity was not found. Posteriorly, the clearing was continued as far as possible, and a large opening was made toward the nose. Healing resulted, and had lasted four years when the report was published.

Microscopic Examination—The tumor consisted of bony trabeculae. These were not broad, but had many well developed osteoblasts. These trabeculae were encountered in sections cut in various directions. Between them was well developed connective tissue, chiefly composed of spindle cells with long nuclei. This tissue did not resemble sarcoma tissue, it appeared in places where normally there was marrow tissue. Atypical cells or myeloplaxes were not found.

CASE 9 (Cauzard, reported by Gagner) —A woman, aged 21, had had a painless swelling for ten years in her right cheek. The skin was normal. An even swelling filled the canine fossa, extending upward to the lower orbital border below to the alveolar process in the region of the molars. It was hard but not tender. The bridge of the nose and the frontal process of the upper jaw were not thickened. The results of examination of the mouth were negative. The alveolar process was thickened on the outer surface. There were carious roots in the place of first two molars. The nose was symmetrical.

Transillumination from mouth outward showed complete darkening of the right upper jaw. A roentgenogram showed marked haziness of the entire body of the superior maxilla. The diagnosis was a paradental cyst (Diffuse hypertrophy was considered but the suggestion was discarded because the condition was unilateral).

Operation—An incision was made in a transition fold from the middle incisor to the wisdom tooth to expose the canine fossa. The walls were markedly thickened, but the maxillary cavity was nonexistent. In its place were masses of spongy bone which permeated the bone without demarcation. The soft tissue was removed without much bleeding or perforation of the inner wall or opening into the nose. The carious roots were extracted and healing followed.

Microscopic Examination—Two different kinds of tissue were found in the tumor. The bony trabeculae of normal structure were separated by fibrous tissue, but marrow tissue was not present. Bony trabeculae were formed of dense tissue, in which osteoblasts were regularly recognized. The intertrabecular tissue was young connective tissue with long cells and small nuclei. Secondary degeneration was not seen.

CASE 10 (Hippel) —A boy, aged 11, healthy and free of all disease, had for four years before he came to the hospital swelling his lower lip and chin. The swelling was a tumor. Some time later he noticed a swelling in the lower cheek. It grew slowly and gradually without pain. About three weeks before he came to the hospital it was noticed that the palate had become thick.

Physical Examination—The skin was normal. There was a swelling of the entire superior maxillary region. The nasolabial fold was obliterated. The swelling was the width of the little finger below the inner angle of the eye, and widened at the left side of the bridge of the nose. It included the mesial two thirds of the zygomatic arch as far as the infra-orbital margin, and extended downward to a line drawn horizontally from the angle of the mouth outward, and lost itself gradually about two fingerbreadths in front of the ear. The skin was freely movable, the surface was smooth, the consistency was bony, without soft spots or parchment crepitation. There was tenderness at only one circumscribed spot over the canine fossa. Irregularities were not present on the lower orbital border, the bulbus did not protrude, and vision was not disturbed. The palate did not divulge on the left side. The upper jaw was evenly swollen from the alveolar process upward beyond the fold of the mucosa, forward almost to the midline and backward over the molar region. The diagnosis was a benign tumor, the nature of which was undecided. A diffuse hypertrophy was thought probable.

Operation—An incision 4 cm long was made from the vestibulum oris outward over the tumor, and flat lamellae of tumor tissue were removed for examination. The spongy tissue was found to be soft without a line of demarcation between it and the healthy bone.

Examination of the patient six months later did not show any change. Transillumination from the mouth outward showed the maxillary cavity, cavity of the eye and the pupil on left side to be dark. A roentgenogram made from the occipito-frontal direction showed darkness of the entire superior maxillary bone.

Microscopic Examination—Irregularly arranged bony trabeculae of various widths were separated by wide, wavy strands of connective tissue. In the fairly homogeneous bony ground substance, some cells were spindle-shaped and some were round. Some had distinct processes. The arrangement of the bone was not lamellary. There were osteoblasts in many places on the margins of trabeculae and osteoclasts in lacunae, more isolated. Connective tissue fibrillae contained numerous cells, mostly spindle-shaped with longish nuclei and isolated round cells, and many distended vessels. There was nothing suggestive of sarcoma. The diagnosis was osteofibroma.

CASE 11 (Uyeno)⁴—A woman, aged 20, who was healthy as a child and came of a healthy family, was troubled with toothache in the upper part of the right jaw at the age of 10. Gradually the right side of the face swelled, without subjective symptoms except occasional toothache.

Physical Examination—A swelling, the size of a man's fist, was found in the region of the upper part of the right jaw. The angle of the mouth was displaced downward and outward and the right eyeball displaced a little forward and upward. The swelling was caused by a tumor of bony hardness with a smooth surface. The skin was normal and movable. The swellings extended on to the zygomatic arch, which was thickened in its mesial half, and to the upper lateral limit of that part of the frontal bone which forms the orbit, and gradually lost itself laterally and superiorly. The floor of the orbit bulged upward, the lower orbital border was rounded off and thickened. In the buccal cavity was found bulging downward, the right half of the hard palate, from which the left molar tooth was missing. It was covered with normal mucous

⁴ Uyeno Beitr z klin Chr 65 (2), 301, 1909

membrane. The tumor was of bony consistency throughout without perceptible crepitation. Glandular swellings were not present. The diagnosis was benign tumor of the upper part of the jaw.

Operation—All bony connections of the upper part of the jaw were severed and the bone was removed. It was found that the bony hard tumor extended far down toward the base of the skull, and here, as well as in the region of the zygomatic arch, many small pieces were chiseled away. Healing was good.

The extirpated tumor measured 9 cm. from top to bottom, the greatest diameter from right to left was 8.5 cm., and anteroposteriorly 7 cm. It weighed 230 Gm. The periosteum was apparently normal. The infraorbital sulcus was indistinct. The demarcation between the alveolar and palatine processes was almost entirely flattened out. The teeth were normal. The tumor was not connected with the roots of the teeth. Toward the nasal wall, the concha nasalis inferior was entirely intact. When the right upper jaw was sawed through it was found filled by a bony mass, without any cavity. The tumor consisted exclusively of bony substance and was spongy. The tumor was softer than normal bone. On the sawed surface of the entire tumor, blood vessels were recognizable.

Microscopic Examination—The tumor consisted of bony trabeculae, some what narrower than in normal bone, with wider meshes between them. These meshes were filled with finely fibrillated connective tissue which replaced entirely the marrow substance. In this connective tissue were numerous blood vessels. In many places there was more connective tissue than fibrous marrow; in other places the contrary was true, so that entire portions of the new formation consisted of fibrous tissue alone. Osteoblasts were found around the bony trabeculae. In the bony trabeculae was an entirely bony structure, particularly large, long, star-shaped bone corpuscles and fine canals, but not of lamellar nature. Results in all the preparations taken from various parts were almost identical. The microscopic diagnosis was *osteofibroma*.

*Case 12 (Ueno)*⁴—A woman, aged 20, six years before examination, had had a severe inflammation of the throat, with swelling of the left angle of the lower jaw, difficult swallowing and fever, lasting three weeks. Soon afterward a swelling of the left cheek was noticed increasing slowly without pain. It reached its full size three years before the examination.

Physical Examination—Swelling of the left half of the face extended upward to 2 cm. below the under orbital margin forward as far as the tip of the side of the nose and losing itself gradually behind. On the upper lip was raised it was seen that the swelling was caused by a tumor on the outer side of the alveolar process of the upper part of the jaw. It began at the left lateral incisor, and extended backward to the last molar tooth. Downward the tumor extended almost to the teeth upward to about 2 cm. from the lower orbital margin. It was covered with normal mucous membrane, its surface almost smooth, its consistency that of bone. The inner side of the alveolar process did not show a swelling.

Operation—A portion of the tumor was first chiseled out. The chisel struck softer bone tissue of almost even consistency, well demarcated from the ground tissue. Microscopically it was like an osteosarcoma. A partial resection of the upper part of the jaw healed successfully.

Microscopic Examination—Pieces of tissue from the tumor at Highmore showed an osteoma, probably produced by an osteofibroma.

CASE 13 (Uyeno) ⁴—This was a case of pedunculated osteofibroma springing from the alveolar process. A woman, aged 47, had noticed a gradually enlarging tumor of the inner side of the left cheek for two years. One year before examination, the tumor began to grow more rapidly. The teeth on that side had been removed some years before for caries. She had difficulty in swallowing, slight pain, and a hanging of the tongue. The speech and mucosa were normal.

Physical Examination—The left cheek was somewhat swollen externally. When she laughed a smooth tumor, covered with glistening mucous membrane, appeared in the left angle of the mouth. On the upper alveolar process there was a tumor consisting of three portions, it extended about 5 cm toward the back and was flattened on the sagittal plane. It was not ulcerated, was not pendulous from a broad pedicle, but hung from the alveolar process, and was movable when touched. The tumor did not involve much of the free surface of the alveolar process, but extended smoothly over the left side of the roof of the mouth a little beyond the midline. Forward, it extended 1 cm in front of the front teeth, behind, not quite to the end of the hard palate. On the plate of the palate also, the tumor could be moved backward and forward. It was covered with mucous membrane, and it was hard, slightly nodular and insensitive.

Operation—The tumor was easily pried away from the alveolar process, and removed in toto. It was attached by a narrow pedicle to the outer lamella of the alveolar process and spread out, like a wing, in various directions. After removal of the tumor, the left alveolar process was removed over an extent of 0.5 cm, leaving a bony defect the size of a phalanx of the thumb. In the posterior angle of the antrum of Highmore was a cyst, the size of a pea, filled with mucopurulent material. That was curetted out, care being taken to spare the mucous membrane of the antrum. Healing followed.

Microscopic Examination—The tumor consisted mostly of wavy strands or irregularly looped fibers of soft connective tissue. There was marked infiltration under the mucosa. In some of these spindle-shaped cells were narrow bony trabeculae. These consisted of different cells, some within the narrow ground substance, were round or oval bone cells with one or two nuclei, others, in the broader ground substance, were star-shaped bone corpuscles. In the margins were also connective tissue cells, which contained much protoplasm. The connective tissue was greater in amount than the tissue of narrow bony trabeculae. Osteoblasts and osteoclasts were not seen. The flat epithelial covering of the roof of the mouth was intact.

CASE 14 (Menzel, Arthur) ⁵—A woman, aged 35, had a large tumor of the lower part of the left jaw for twenty-five years. It started, according to the patient, in the region of the lower first molar tooth, and in five years had become twice the size of a man's fist. Twenty years before this examination, Balassa had begun to operate on it, but had been forced to stop because the patient had a dangerous fainting fit. The tumor had grown steadily since then. Ten years before, the patient had begun to limp on the left leg. The family history was negative.

Physical Examination—The tumor was the size of a child's head, occupied two thirds of the lower jaw, and extended as far down as the cricoid cartilage, where the skin passed over directly on to the tumor.

The malar bone was forced upward by the tumor. The mouth was drawn out to three times its normal length. From the mouth projected a tumor nodule the size of a fist, on the anterior periphery of which was a roughened surface with traces of alveolae. The buccal cavity was so filled out by the tumor that the left palate was forced upward for a considerable distance. The posterior border of the ramus extended to the posterior pharyngeal wall but was not adherent to it. The lower jaw was mobile, but within only slight limits. Two scars traversed the tumor, from the angle of the mouth to the region of the articulation of the jaw, forming an ellipse (scars of old uncompleted operation?). Within the ellipse the skin was entirely immovable elsewhere it was mobile. The tumor was of firm consistency on the outside and toward the mouth it was of bony hardness. The diagnosis was a calcified encysted sarcoma.

Operation—The operation was recognized as dangerous but was proposed and the patient agreed to it, otherwise the tumor would soon have compromised respiration and the taking of nourishment.

The jaw was sawed through in the region of first molar tooth on right side. Two incisions were made, from the left angle of the mouth over the great convexity of the tumor to the articulation of the jaw parallel to those of Balassa, but half an inch farther out. The entire outer surface of the tumor was exposed by dissection of the skin in long strips. The extremity of the jaw which had been sawed was then seized and drawn outward and the soft parts pushed away.

The insertion of the tendon of the temporalis was four times its normal width and had to be cut. The disarticulation of the joint occurred spontaneously from the weight of the tumor. Hemorrhage was comparatively slight. Spontaneous retraction was expected to shorten the greatly lengthened lower lip. Recovery and healing was good at first. Erysipelas developed in the right cheek one week after operation, and the patient died on the thirteenth day after operation. Autopsy showed that the erysipelas was the sole cause of death.

Description of the Tumor—The tumor was almost wholly bony. It weighed after removal of soft parts, more than 3 pounds (1.4 kg.). The body of the mandible was so increased in height that the ramus was almost completely included in it. The periosteum which was much thickened on the inner side peeled off easily. On the outer side, even the skin adhered firmly to the bone by the medium of a hard white fibrous mass. The nervus alveolaris inferior, the nervus mentalis and the corresponding canal were undisturbed. The distance through the intramaxillary canal was 2.5 cm. (normal distance 1.0 cm.). The nerves were not markedly changed microscopically. A cross section through the lower jaw, forward through the coronoid process of the mandible and the glenoid fossa of the temporal bone, showed a hard bony center surrounded by a layer, varying in thickness, and composed of a white fibrous tissue surrounded in turn by the extremely expanded cancellous substance of the mandible. The central part was irregular and was composed in the middle of substance resembling that of the epiphysis and periphery of more compact substance.

The fibrous tissue was thickest internally. It included the coronoid process of the mandible with touchable processes.

The outer bony covering, presumably the expanded body of the mandible, above was widest posteriorly and had a rough surface. The cancellous tissue in the latter near the posterior margin was very coarse and irregular. Embedded in the bone the crown of a lower molar tooth was seen, but no other bud.

A cross-section from the outside inward showed a porous substance, the rather large pores filled with fibrous reddish masses. The fibrous masses were arranged in alveolar fashion like the diploe of the tumor.

Microscopic Examination—The peripheral fibrous layer and the alveolar nodules both consisted of connective tissue. In the peripheral layer the fibers were mostly fine, straight and in thick bundles. In other places the bundles were thinner and arranged in meshes. In a few places the corpuscles were filled with brown granular pigment over considerable stretches. Isolated among the fibers were single, larger, slightly turbid cells which had large, oval nuclei with sharp contours. The meshes were filled with connective tissue or homogeneous intercellular substance and star-shaped anastomosing corpuscles.

The structure was not markedly different in the central larger soft masses, or in the numerous large and small nodules and veins that traversed the bony mass in all directions. It was also composed of connective tissue which appeared in various forms. Alveolar structure predominated. The fibers were sometimes fine, sometimes thick, and were parallel to each other. In places they were covered with a fine dust, elsewhere they were hyaline and brittle. A lymphadenoid network, sometimes thick, sometimes delicate, was spread between the meshes, and corpuscles were not noticed at points of intersection. This network had a tendency to pick up lime molecules, so that few were found free from it. A finely dusted over membrane seemed to be stretched between the connective tissue trabeculae.

Frequently the margin of the bundles of connective tissue had a homogeneous, light refracting, yellowish border. From this sprang hyaline buds, which sent out other buds, so that some meshes were filled with proliferations resembling a bunch of grapes. Some of the separate "grapes" were loose. Some were composed of many layers and resembled the granules of psammoma.

In some places the alveolar structure gave way to a connective tissue with faintly indicated fibrillation. Occasional stiff fibers took the form of the skeleton of a leaf.

Many deposits of lime, as dust or as larger particles, were in the connective tissue. The hard portion of the tumor, by far the largest part, offered only the picture of normal bone with abundant provision of haversian canals and concentric arrangement of bony layers. There were large numbers of bone corpuscles, usually round, mostly raved, sometimes with the long rays running exclusively parallel to one another, as in tooth cement. These bone cells were particularly well developed in the diploetic substance. A nucleus was frequently demonstrable in them. In the diploetic substance was reddish marrow, consisting of lymphoid cells. In the larger spaces there were fat globules, in the large ones, particularly in the center of the tumor, were found the soft tumor masses above described.

The tumor was considered an osteoma because the greater part consisted of pure bone tissue, but examination of the inconsiderable soft portion classified it genetically as a fibroma. Calcification and ossification are particularly frequent in tumors of the jaw, though often incomplete and comparatively unimportant. This seems to be the first case reported in which so large a tumor was composed almost wholly of well formed bone. The chief growth of the tumor took place between the second and third molar teeth.

CASE 15 (Maclaure and Maurel) —The patient was a woman who was admitted to the hospital on Dec 9 1912 for an ectopic placenta. In addition to the uterine lesion she had a tumor the size of a walnut at the angle of the right lower jaw. This tumor was large and of a firm consistency. It was not adherent to the superficial structures, was not painful spontaneously or on pressure and was not inflamed or ulcerated. It developed externally.

The tumor began to grow about twenty years previously. It grew progressively, and never was painful. All the teeth were normal. A diagnosis of osteoma was made.

She died three weeks after admission. Death was due to hemorrhage from the uterus. At autopsy, the horizontal branch of the maxilla, the symphysis, and the right half of the lower jaw was distorted.

The tumor was rounded, the external surface was convex and was the color of bone. The surface was regular but with some small elevations and depressions. On the internal surface the tumor was entirely reabsorbed. Above this level the tumor was hollow, forming a deep cavity. The internal surface of the cavity was irregular and hard. The condyle was rough and irregular, also the coronoid process. The size of the tumor was 7 by 6 by 4 cm.

Histologic examination showed that the tumor was composed of osseous tissue with islands of osseous tissue. It resembled a fibroma.

CASE 16 (Monmer L.) —In a boy aged 15 in 1911 a tumor developed on the lower gum a little to the right of the median line. It grew progressively and was painless. In 1912 a temporary fistula developed at the level of one of the lower incisors. The tumor developed in the alveolar bone and was not treated except by punctures at various times.

When the patient was admitted to the hospital on October 1912, a pronounced protrusion of the chin which was greater on the left than on the right. The skin was healthy.

With the mouth opened the lower gum seemed to be normal. The mucosa was covered with normal mucosa. The patient did not have any pain.

The tumor was firm but was more fibrous in its median portion and more osseous at the sides. There was one point of softening, at the second incisor where the punctures had been made. The tumor was 4 cm long and 3.5 cm wide. It was absolutely painless. Mastication was possible except for hard foods.

On October 10 a dentist fitted two rims fixed by bands to the lower molars on each side. An operation was performed under ether anesthesia on the next day. A horseshoe incision was made over the tumor.

to the molars. This appliance maintained the normal separation of the ends of the maxilla.

The postoperative course was normal, without pain or fever. The sutures were removed on the sixth day, and healing was complete on the ninth day. The scar was scarcely visible.

CASE 17 (Wylie, A)⁸—A man, aged 53, consulted Dr. Wylie on January 9 complaining of a growth in the palate of twenty-five years' duration. He did not feel any pain and little discomfort, in fact, he said that beyond a certain amount of anxiety it was not troublesome, and, since it had grown slowly and gradually, he had become used to it. Mastication and deglutition were performed without any difficulty, and with the exception of a slight thickness or impaired resonance, his voice and articulation were normal. He had always had perfect health, and his teeth were sound. On examination, a large, smooth, oval swelling was seen occupying the whole of the hard palate. It was the same color as the surrounding mucus, it was not tender to the touch, was firm and slightly movable on steady pressure. Without employing any anesthetic, it was removed by an ordinary polypus snare, and the stump healed rapidly. Dr. Wylie had waited eleven months to see whether there was any recurrence.

Dr. Wyatt Wingrave reports: "The tumor has the appearance of a new potato, it measures 5 to 2.8 cm and weighs 13 Gm. The cortical part, for a depth of about 5 mm is firm and tough, and encloses a hard, stony core, which reaches the surface at its point of attachment. In structure, the cortex is composed of densely packed white fibers mingled with elongated fusiform cells (fibroblasts). The stonelike core consists of compact bone with relatively small cancellous spaces, resembling ivory or petrous bone. It is evidently an osteoma growing from the periosteum of the maxilla, to which it was attached. There is no sign of any sarcomatous tendency."

COMMENT

The three cases that I have reported, together with those collected from the literature, comprise a group of seventeen cases in all. In reviewing this small group, the four cases spoken of by Hildebrand must be omitted on account of lack of details about them.

Many of these tumors begin in childhood, although the patient may not apply for treatment until adult life. Hippel says that they start between the ages of 7 and 14. In eight cases in this series, the onset was in youth, but in five cases it was well on into adult life. The most advanced age of onset was 54, the youngest was 7.

It is difficult to say much about the influence of sex, as eight of these patients were women and five were men. There was a previous history of carious teeth or an inflammation about the jaw in five cases. In two other cases the patient gave a history of an injury of the face previous to the appearance of the tumor.

The symptomatology of these tumors is that of a slow growing, painless tumor that involves either the upper or the lower jaw. By its size or position it may interfere with the action of the jaws, but the nasal

⁸ Wylie, A. J. Laryngol Rhinol & Otol 24:30 (Jan.) 1909.

Microscopically, differentiation is easy except in the case of leontiasis ossea. Hippel says that Bordenhauer's description of his case of leontiasis ossea agrees exactly with the histology of osteofibromas. Only the clinical picture can differentiate the two processes.

The prognosis is generally favorable. These tumors are benign, and do not tend to recur after thorough removal. They grow slowly, and it is not known whether they ever reach a spontaneous standstill.

The only treatment advisable is a complete surgical removal of the tumor. In most instances a line of demarcation can be found, and the tumor can be enucleated or curetted out. Resection of the bone is not necessary, except in the case of extensive growths. For the extensive tumors, a preliminary ligation of the external carotid artery will be of material aid in simplifying the technic.

On admission he was in a comatose condition, but had good color. There was a scar in the left frontal region. The blood pressure was, systolic, 120, diastolic, 80, and the pulse rate was 90. There was a lateral nystagmus of both eyes, but otherwise the cranial nerves were apparently normal. Breathing was abdominal. The pectoral muscles and the right upper extremity were spastic, with increased reflexes. The epigastric and cremasteric reflexes were normal. Patellar reflexes were exaggerated on both sides. He did not show abnormal sensory signs. The spinal fluid was clear, under normal pressure and contained 2 cells per cubic millimeter, without any increase of globulin. The result of the Wassermann test was negative. The coma became deeper three



Fig 1—Inner surface of the dura in case 1, showing membrane covering left hemisphere

days after admission, and signs of pulmonary congestion appeared. Death occurred two days later.

Autopsy—The dura was unusually adherent to the skull, especially over the left parietal region, where it was brownish red and appeared thickened. The inner surface of the dura on this side was covered with a layer of dark reddish brown, organizing blood clot which extended over almost the whole of the left hemisphere (fig 1). The average thickness near the center of the clot was 4 mm, and it became gradually thinner toward the margins. The inner surface of the clot was a thin, glistening, semitransparent membrane, apparently

against advice, saying that she felt well. Nine days later she became irrational, and was readmitted to the hospital. Neighbors said that she had changed considerably since she was injured, and had been despondent for about five days.

There were ecchymoses about the left frontal region and the left eye, a systolic murmur at the apex and contracture of the toes of the right foot. The lower portion of the left seventh cranial nerve was slightly weak, and the tongue protruded to the left. The patellar reflex was increased on the left. The pulse rate was 105, the temperature 99.4 F and the respiration 40. The blood pressure was, systolic, 180 and diastolic, 105. The spinal fluid was slightly xanthochromic, under normal pressure and did not contain an increase of cells or globulin. The result of a Wassermann test of the spinal fluid was negative. A second roentgen-ray examination at this time showed that the skull was not fractured. The patient's condition remained unchanged until death four days later.

Necropsy was limited to the head. The pupils were equal and regular, 4 mm in diameter. There was a hematoma of the scalp 2 cm in diameter above the outer angle of the left eye, and there were ecchymoses about the left eye and in the left submaxillary region. Beneath the dura on the right was a dark red blood clot apparently beginning to organize. This clot extended from the base in the middle fossa to the vertex and about 4 cm anteriorly and posteriorly from the middle branch of the middle meningeal artery. There was a small amount of blood in the right subarachnoid space, although the arachnoid was not injured. The cortex beneath the clot had a slight yellowish tinge. The skull was not fractured. The comparatively recent clot beneath the dura was undergoing organization in the portion next to the dura. Granulation tissue in the organizing clot contained many leukocytes, mostly endothelial, filled with red blood corpuscles and blood pigment. There were many capillaries and large spaces lined with endothelium. Some of these spaces contained blood. The pia mater was infiltrated with leukocytes, mostly endothelial, filled with blood pigment, but also many lymphocytes. The lumen of one artery in the pia contained a mass of firm, fibrous tissue almost obliterating the lumen. Van den Bergh tests on the liquid portion of the clot did not show an increase of bilirubin over that of blood from the heart.

CASE 3—Traumatic subdural hematoma of two months' duration with recurrence of symptoms

B. H. C., a white man, aged 54, was first admitted to the hospital in a semi-comatose condition on May 31, 1926. About two weeks previously he had struck his left frontal region against an open door. He was unconscious for a time, and afterward complained of constant, dull headache and general weakness. This continued until the day of admission, when he was found in a stupor.

The pupils were equal and regular, reacting normally. The result of the ophthalmoscopic examination was negative, and the cranial nerves did not show disturbance. Contractures, spasms or paralysis were not present. Biceps and patellar reflexes were active, especially on the right side. Abdominal reflexes were not elicited. Both achilles' tendons were active, and there were suggestive Babinski and Oppenheim signs on both sides. Temperature, pulse and respiration were normal. The blood pressure was 170 systolic and 90 diastolic. The spinal fluid was clear and under normal pressure. The amount of globulin was not increased. There were 6 cells per cubic millimeter of fluid. Results of a Wassermann test were negative. The patient's mental condition gradually



leukocytes were found in the outer portions of the cortex. The van den Bergh test applied to the liquid portion of the clot showed six units of bilirubin. Control of the serum from the blood of the heart showed 0.2 units. Other anatomic observations were pulmonary congestion, chronic splenitis and healed perihepatitis.

CASE 4—*Subdural hematoma without history of trauma* J. C., a negro, aged about 40, was admitted to the hospital on Aug. 15, 1926, unable to talk. There was weakness of the entire right side. He had complained of persistent, dull headaches for some time, but had been well otherwise until three days before he was admitted. Relatives said that he was a heavy drinker, but a history of injury to the head could not be obtained.

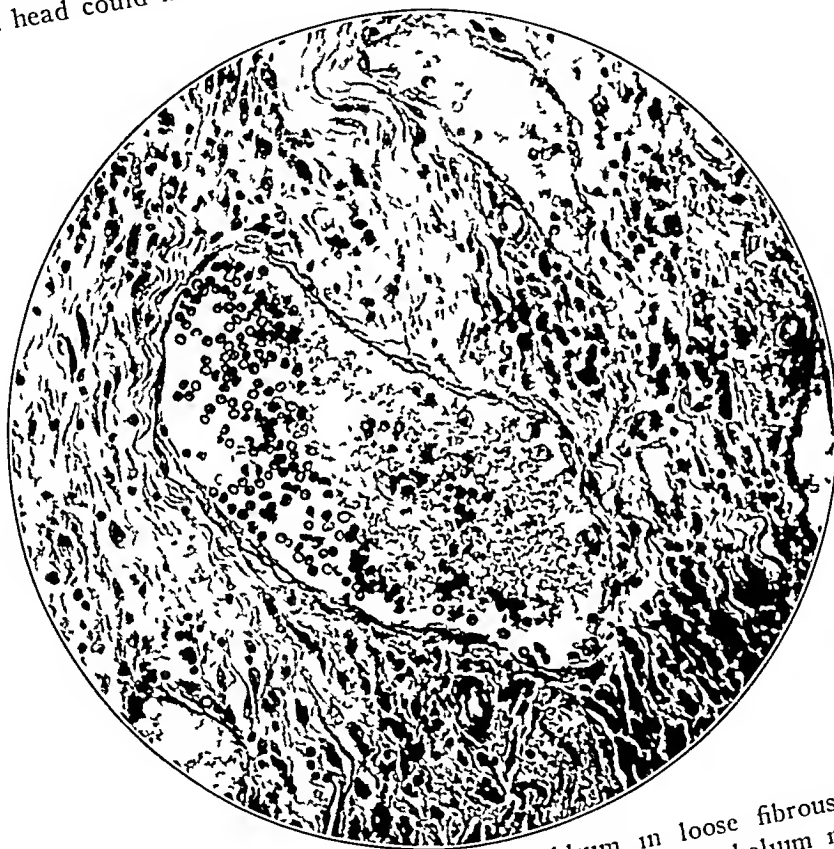
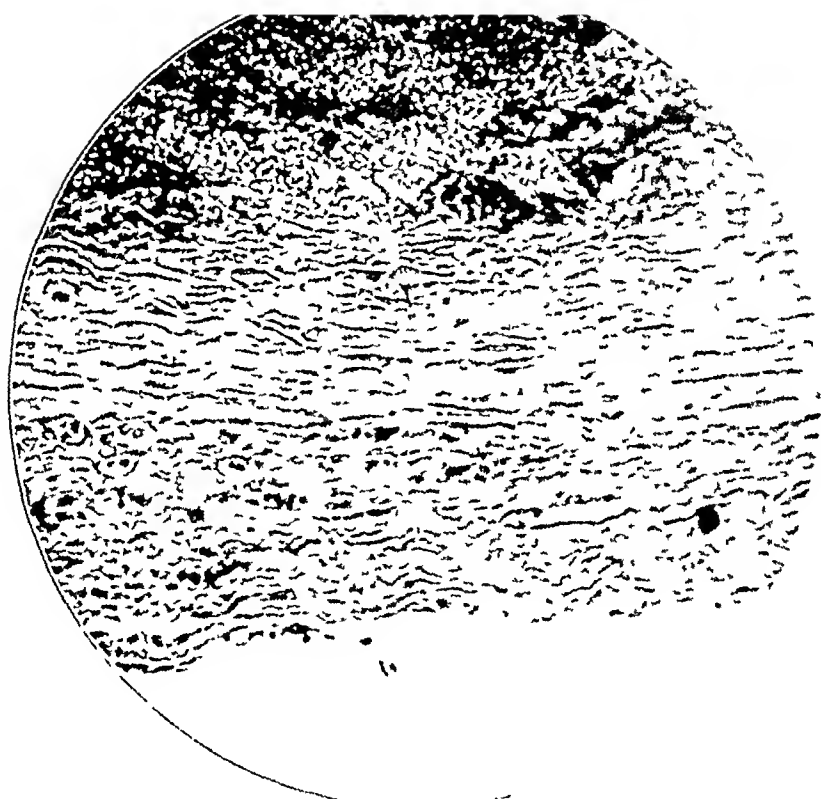


Fig. 4—Large spaces lined with endothelium in loose fibrous tissue just beneath the dura. The irregular formation of the endothelium may be seen. $\times 210$

The lower portion of the left seventh cranial nerve (supranuclear) was weak. The tongue protruded to the left. The right arm and leg were decidedly weaker than the left, but did not twitch or jerk as did the left arm and left pectoral muscle. Tendon reflexes were hyperactive on the right. There were Babinski and Oppenheim signs and ankle-clonus on the right. The spinal fluid was clear and under normal pressure. The amount of globulin was not increased. There were 50 mononuclears per cubic millimeter. The result of the Wassermann test was negative. Three days after admission the patient was able to mutter a few words and weakness on the right side was less pronounced but death occurred the following day.



CASE 5—*Pachymeningitis hemorrhagica interna*

S M B, a white man, was admitted to the hospital, unconscious, Feb 1, 1915. He had been a rather heavy drinker for ten years. About a month before admission he began to have severe headaches. Two weeks later he lost consciousness for about two hours. At this time his speech was unintelligible, but paralysis was not noticed. The day before admission he fell and lost consciousness, during the night general flaccid paralysis of the upper and lower extremities developed. On admission the right pupil was dilated and fixed, the left pupil contracted and fixed. There was a slightly choked disk. Both arms were flaccid, especially the left. Patellar and elbow reflexes were absent. The Babinski sign was positive. He showed Cheyne-Stokes respiration, and there were moist râles over both lung fields posteriorly. Death occurred nine hours after admission.

At necropsy the left cerebral hemisphere was covered with clot, and on the left, anterior to the fissure of Rolando was similar material mixed with thin, grayish fluid. The cortex beneath these areas was slightly depressed. The inner surface of the dura was covered with similar grayish membrane which stripped easily from the layer of clot beneath. Beneath the dura was a layer of rather loose fibrous tissue which was infiltrated with leukocytes, including endothelial cells, filled with blood pigment, lymphocytes and a few polymorphonuclears. This tissue contained numerous capillaries and large spaces lined with endothelium, some containing blood. In and beneath this layer were large areas of old hemorrhage undergoing organization. Sections of the cortex beneath the clot showed thickened and congested pia mater and arachnoid with marked reaction of polymorphonuclear leukocytes, lymphocytes and pigmented endothelial leukocytes.

CASE 6—*Pachymeningitis hemorrhagica interna*

E T, a colored man, aged 75, was admitted to the hospital on Nov 17, 1916. The history was not obtainable. The patient was unconscious and cyanotic, and the respiration was labored. Sounds of the heart were not audible, nor was the radial pulse palpable. The pulse rate (abdominal aorta) was 68. The pupils were dilated, but ten minutes later contracted. They did not react to light. Reflexes were absent. The percussion note was dull over the posterior portions of both lungs. The patient died two hours after admission.

At autopsy the inner surface of the dura over the left hemisphere was covered with a dusky red, soft, glistening membrane which could not be peeled off. There were a few small, similar areas on the right, posteriorly. Convolutions beneath the membrane appeared dull and slightly flattened. Beneath the dura was a thin layer of dense fibrous tissue containing elongated, endothelial-lined spaces, some filled with blood. Pigmented endothelial leukocytes were fairly abundant. Fibrous strands from this layer invaded a layer of old blood clot, but there was little active organization, many lakes of clot being encapsulated by dense fibrous tissue. The inner layer was a thin membrane of dense fibrous tissue lined with endothelium. Other pathologic observations were lobular pneumonia, chronic myocarditis and chronic nephritis.

CASE 8—*Pachymeningitis hemorrhagica interna*

C B, a colored man, aged 55, was first admitted to the hospital on Aug 17, 1918. He had used considerable liquor until two years before admission. The complaint was precordial pain. The reaction to the Wassermann test was ++++. A diagnosis of aneurysm of the descending arch was made. He was discharged on September 22, but was readmitted on Jan 12, 1919. Further

There were no histologic differences between the cases with history of trauma, and those in which such history was not elicited. In the recent, actively organizing clots the endothelial cells lining the cystic spaces were more scattered and irregular, capillaries were more numerous, and fibrous tissue was looser than in the older and more fully organized clots (fig 6). In general, the clots in cases without a history of trauma appeared older and more nearly healed. However, the patients in cases 1 and 3, with definite relationship to trauma, had older and better organized fibrous tissue and endothelium than those in



Fig 6—Empty space lined with endothelium in case 6. Fibrous tissue is dense and well organized. Endothelium is well developed and regular. Some endothelial cells seen on the flat appear plump, $\times 210$.

cases 4 and 5, in which there was not a history of trauma. We believe that features, such as development of endothelium, which are usually considered as differentiating chronic subdural hematoma and chronic pachymeningitis hemorrhagica interna, are rather differences in degree of organization than differences in type.

The high concentration of bilirubin in two of these clots (thirty and twenty times that in the blood from the heart) and crystals of hematin in others indicates that bile pigment is formed during their

mental derangement is a result rather than a cause of chronic subdural hematoma. The degree of trauma necessary to produce this lesion, not sufficient to cause fracture in any case in this series, may be so slight that it requires special effort on the part of the examiner and the patient to obtain a history of injury. In the old case in the alcoholic patient and in the insane person it is especially difficult to get such information. It is probable that most, if not all, cases, of so-called spontaneous pachymeningitis hemorrhagica have a beginning in a forgotten injury.

Symptoms of chronic subdural hematoma as presented by Putnam¹ fall into two classes: first, those due to general increase in intracranial pressure, as headache, vertigo, vomiting, slow pulse and choked disk; second, those due to local disturbances as paralysis, sensory disturbances (rare), convulsions and aphasia. In addition, there may be those of meningeal irritation, as stiff neck. These signs may occur in almost any combination, and, besides being variable and fleeting, are likely to be atypical and incomplete. In this series a latent period, of varying length, was the rule. Headache followed by vertigo, vomiting, psychosis and coma is the common course. Choked disk was not found in the four cases recently observed, and was indefinite in case 5. It is often surprising that there are so few physical observations. Terminal lobular pneumonia is common. Increased reflexes, spasticity of various muscle groups and disturbances of the third and fourth cranial nerves are the chief neurologic observations. The spinal fluid is usually normal in all respects, though it may be xanthochromic, or it may contain blood in those cases in which the arachnoid is injured. The temperature varies little from normal, though it is usually slightly subnormal toward the end. The pulse is often a pressure pulse.

Diagnosis depends on a history of cranial trauma, often slight, followed by a variable latent period. It may be impossible to elicit history of injury. Following this is a period of headaches, continuous or intermittent, increasing in severity, then psychosis, coma and death. If the diagnosis is made early and surgical treatment instituted, the prognosis is fairly good.¹

CONCLUSIONS

1 Chronic subdural hematoma and pachymeningitis hemorrhagica interna are the same, clinically and pathologically.

2 Both probably have their origin in trauma, with some predisposing vascular lesion as a factor.

3 Trauma, headache, psychosis and coma is the usual sequence with additional variable neurologic signs.

4 This condition should be considered in patients presenting this series of symptoms and surgical treatment instituted if indicated.

5 The lining cells of the meninges are probably potential members of the reticulo-endothelial system.

pressure decreased, a bradycardia developed which was later replaced by an arrhythmia. These effects were eliminated either by division of the vagi or by the administration of atropine. They next prepared bile salt of biliverdin was found to be nontoxic. As a 20 per cent increase the latter reproduced the results obtained with whole bile. The calcium salt of biliverdin was found to be nontoxic. As a 20 per cent increase in the calcium of the blood was observed during the experiments, it was concluded that calcium was protective against toxic bile pigment.

The conclusion attributing the toxicity of bile to the pigment is difficult to reconcile with certain known facts. In early obstructive jaundice and in rapidly occurring hemolytic anemias there may be a great accumulation of pigment in the tissues and plasma without any of the symptoms of bile toxemia. On the other hand, bile peritonitis clinically and in experimental animals may be lethal before even the sclerae are tinged with bile. Were the toxicity of bile due to pigment alone and the lack of symptoms in jaundice due to the pigment being combined with calcium, then there should be a parallelism between the calcium of the blood, the van den Bergh reaction of the blood and the symptomatology. This has not been observed. In obstructive jaundice there is a large output of bile pigment in the urine without a similar rise of the calcium, however the output of calcium in the feces is increased.⁶ This necessitates the conclusion that there is considerable toxic uncombined pigment constantly in the circulation or that the kidneys have the power of splitting the calcium from the calcium pigment molecule. Such a function of the kidney has not been demonstrated.

It would seem, therefore, that in obstructive jaundice the bile in the blood stream may be detoxified by some organ, or there may be a depression of the function of the liver, and all the normal elements of bile may not be escaping into the circulation. With this conception, in view of the work of Mann,⁷ Rich⁸ and others concerning the extrahepatic formation of bile pigment, the degree of deposition of pigment would not necessarily be an index of the toxemia. This is nearer in accord with the clinical facts.

DETOXIFYING ACTIVITY OF THE LIVER

There is a great deal of evidence showing that the liver is capable of destroying certain soluble toxic substances. Buys⁹ incubated emulsions

6 King J. H., Bigelow J. E., and Pearce, L. Experimental Obstructive Jaundice, *J. Exper. Med.* **14** 59, 1911.

7 Mann, F. C., Sheard C., Bollman, J. L., and Baldes, J. The Site of the Formation of Bilirubin. *Am. J. Physiol.* **74** 497 (Nov.) 1925.

8 Rich A. R. On the Extrahepatic Formation of Bile Pigment, *Bull. Johns Hopkins Hosp.* **36** 233 (April) 1925.

9 Buys, E. Contribution a l'etude de l'action destructive exercee par le foie sur certains alcaloides. *Ann. Soc. Roy. d. sc. med. et nat. de Bruxelles* **4** 73, 1895.

would be more or less uniformity from day to day. The material was diluted with an equal volume of physiologic sodium chloride and injected within three hours after its collection. Each specimen of bile was used for two experiments: in one the injection was made into a systemic vein, while in the other a branch of the portal vein was used.

Dogs were used in all experiments, and an effort was made to obtain two animals of approximately the same weight to test a single specimen of bile. The dogs were anesthetized by the open drop method, and later a cannula was placed in the trachea and connected with an ether bottle. The peritoneal cavity was then opened and a needle connected with rubber tubing to a buret was inserted and tied either into a branch of the mesenteric vein or into the iliac vein, depending on the experiment. This insured an equal amount of intra-abdominal manipulation in each type of experiment. A cannula was placed in the carotid artery and connected with a mercury manometer for a blood pressure tracing. A tube was placed in the etherization system and connected with a tambour and writing lever for a tracing of the respiratory movements. The femoral artery was then exposed for the taking of specimens of blood. Bile diluted with an equal volume of physiologic sodium chloride was injected from the buret at a uniform rate of from 2.5 to 3 cc per minute. Blood pressure and respiration tracings were made after the injection of every 25 cc of diluted bile. Specimens of blood were taken previous to the beginning of the injection, after each 50 cc injected, and finally at the end of the experiment. Quantitative van den Bergh¹⁶ and calcium¹⁷ determinations were made on the blood. In some experiments the vagi were divided to determine the effect on the cardiac arrhythmia.

RESULTS

Ten specimens of bile were tested in animals in whom the vagi were intact. Figure 1 shows the characteristic gradual fall of blood pressure which occurs when bile is injected into a systemic vein. This fall in blood pressure is later accompanied by a striking arrhythmia, and at times there is an apparent cessation of cardiac activity. Figure 2 shows the characteristic blood pressure curve when bile is injected into a branch of the portal vein. The fall in blood pressure and arrhythmia are identical with that seen in figure 1. In both curves the alterations in respiration are quite similar.

The results are summarized in table 1. The lethal dose when given into a systemic vein varied from 6.5 to 12.3 cc per pound of body weight, while when given into the portal vein the lethal dose varied from 6.4 to 13.9 cc per pound. The average lethal dose in the systemic vein was 8.8 cc while in a branch of the portal vein it was 10.04 cc per pound of body weight. This is approximately 13 per cent more in the portal than in the systemic circulation. In all the experiments tabulated, with

16 McNee J. W. Jaundice: a Review of Recent Work, *Quart J Med* 16:390 1923.

17 Clark E. P. and Collip J. B. Tisdall Method for Determination of Blood Serum Calcium with a Suggested Modification, *J Biol Chem* 63:461 (March) 1925.

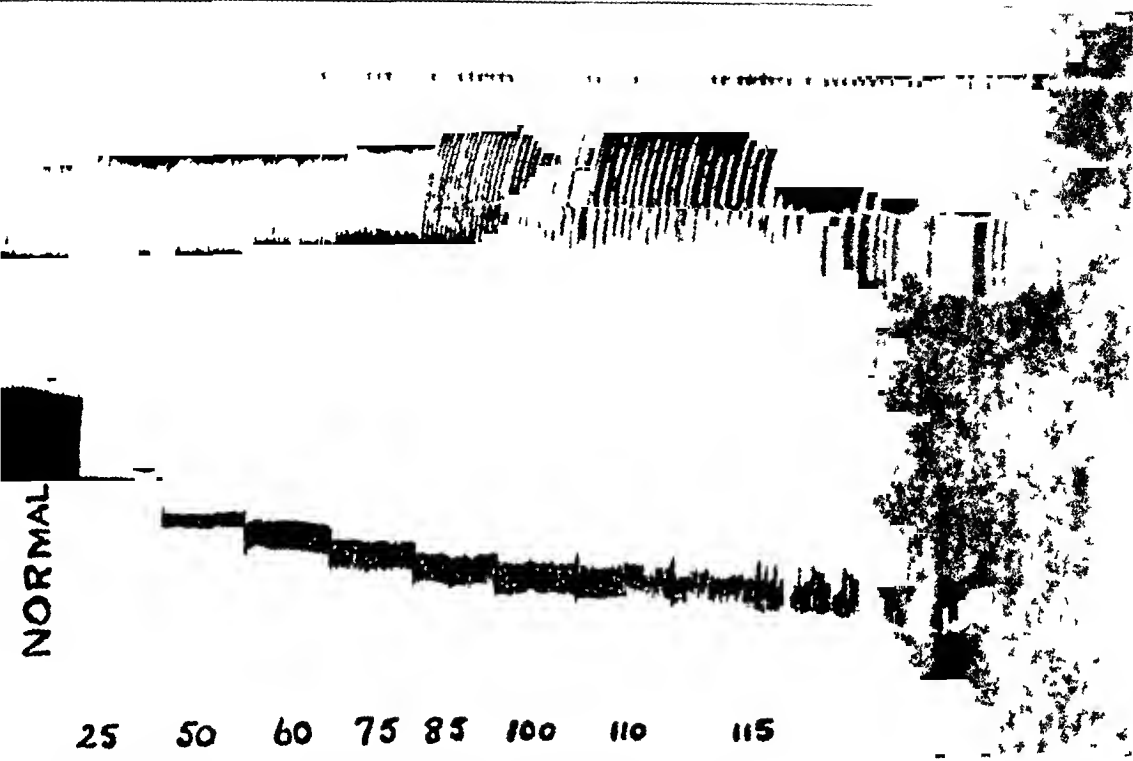


Fig 1—Effect of injection of bile into a systemic vein on the blood pressure. The signs are intact.

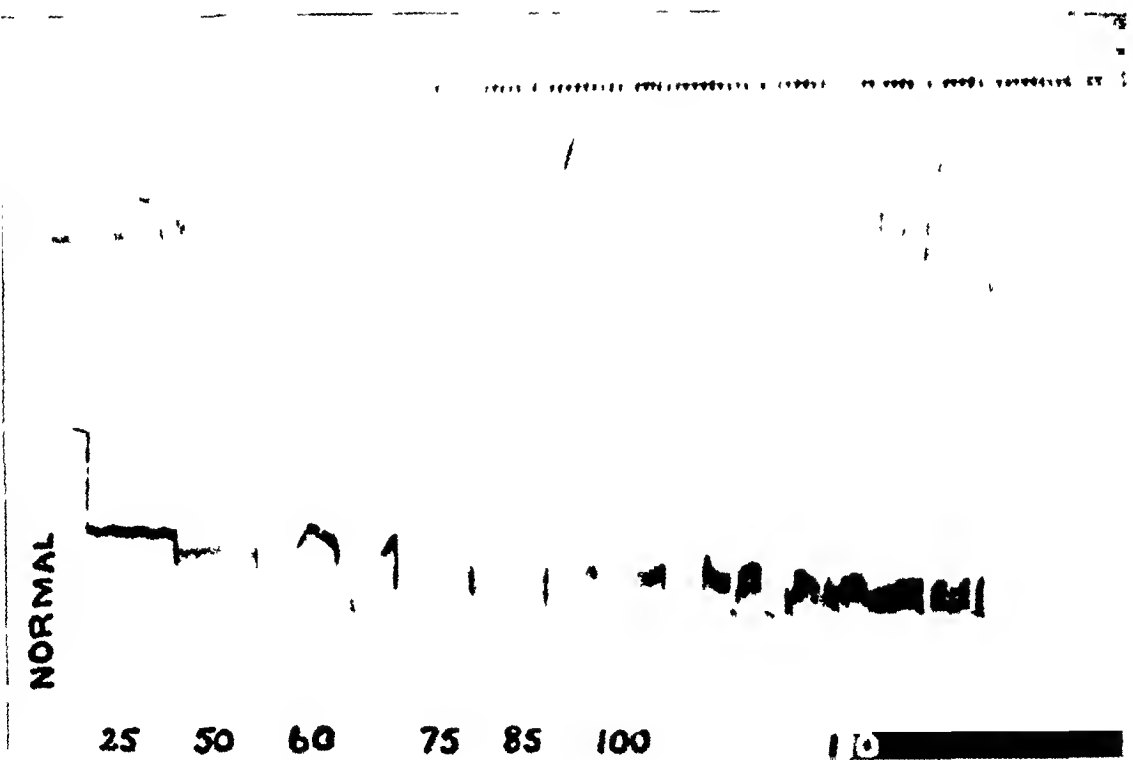


Fig 2—Effect of injection of bile into a systemic vein on the blood pressure. The signs are intact.

TABLE I—Vagi Intact

Bile Specimen	Systemic Vein					Portal Vein				
	Weight of Dog, Pounds	Amount Injected, Cc	Serum		Lethal Dose per Pound, Cc	Weight of Dog, Pounds	Amount Injected, Cc	Serum		Lethal Dose per Pound, Cc
			Calcium at Beginning, per 100 Cc, Mg	Calcium at End, per 100 Cc, Mg				Calcium at Beginning, per 100 Cc, Mg	Calcium at End, per 100 Cc, Mg	
1	10.25	108	—	12.0	—	182	11.1	25.1	—	12.7
2	22.0	118	8.0	18.8	—	213	8.0	17.0	—	10.1
3	15.0	100	11.2	12.0	—	209	12.1	21.0	—	12.1
4	26.5	278	7.1	8.2	—	177	8.8	10.3	—	10.1
5	27.5	100	11.0	10.0	3.8	110	10.0	19.3	0	13.9
6	17.25	136	8.0	10.2	1.6	127	8.1	13.7	0	6.6
7	1.5	102	11.8	11.1	0	127	10.6	11.3	0	7.1
8	19.0	188	11.0	19.2	0	220	7.0	13.6	0	11.0
9	19.0	128	10.0	12.1	0	79	11.1	16.2	0	1.2
10	11.5	118	11.8	13.6	0.8	121	13.8	14.8	0	9.8
Average			10.9	13.7	1.9		10.7	10.6	0	2.1
					8.8					10.01

TABLE 2—Vaghi Divided

Bile Specimen	Weight of Dog, Pounds	Systemic Vein					Portal Vein							
		Amount Injected, Cc	Serum Calcium Beginning, per 100 Cc, Mg	Serum Calcium at End, Mg	V in den Bile, mg	T ethal Dose per Pound, Cc	Weight of Dog, Pounds	Amount Injected, Cc	Serum Calcium Beginning, per 100 Cc, Mg	Serum Calcium at End, Mg	V in den Bile, mg	T ethal Dose per Pound, Cc	Bile Calcium per 100 Cc, Mg	
9	11.5	58	13.6	10.8	0	5.0	29.5	237	11.6	16.1	0	1.5	8.0	10.8
10	6.75	24	13.1	12.2	0	3.5	11.0	11	12.2	13.2	0	1.6	1.0	9.8
11	23.0	12	12.3	11.2	0	5.7	20.75	80	11.1	11.6	0	0.6	1.3	9.0
12	11.0	58	11.0	11.6	0	5.2	13.25	80	11.0	11.1	0	0.0	6.0	9.6
13	11.5	84	15.1	11.6	0	5.4	19.75	138	11.6	11.2	0	0.2	7.3	10.1
14	17.0	157	15.1	11.0	0	9.2	21.5	180	12.1	11.8	0	1.5	8.3	9.6
Average			13.1	12.9	0	5.7			13.0	13.0	0	0.9	6.3	

VAGI DIVIDED

Six specimens of bile were tested in animals after division of the vagi to determine whether the arrhythmia could be duplicated by this procedure. The results are summarized in table 2. The average dose given into a systemic vein was 57 cc. and in the procedure

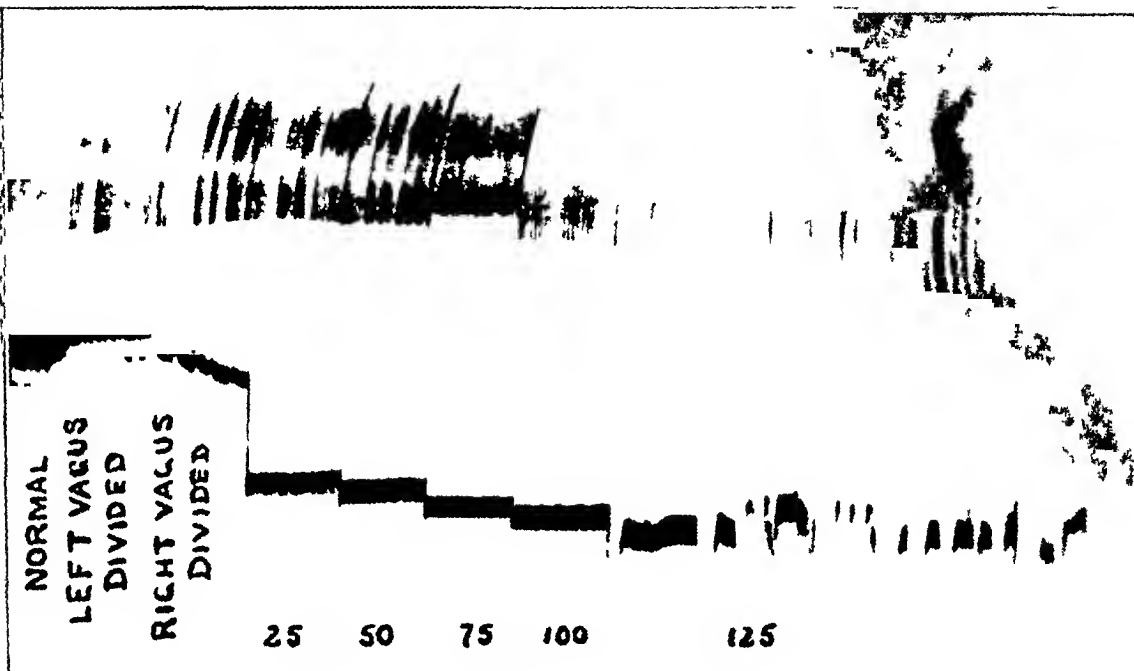


Fig. 3- Effect of injection of bile into a systemic vein

bile is injected into the portal vein with the vagi divided. This curve is similar to that seen in figures 1, 2 and 3.

COMMENT

The fact that the lethal dose of bile given at a uniform rate is 13 per cent higher when injected into a branch of the portal vein than when given into a systemic vein does not necessarily indicate that the bile has been detoxified by the liver or that some toxic element has been removed. It is generally believed that death in such experiments is due to direct action of bile on the myocardium. In those experiments in which the bile was injected into the iliac vein, it was carried directly to

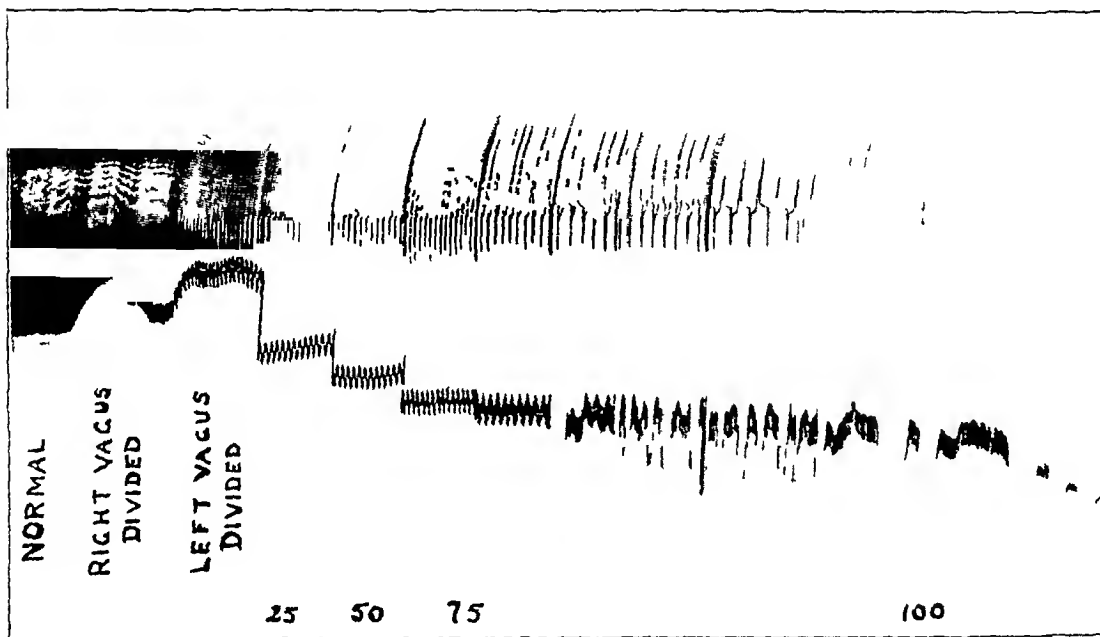


Fig 4—Effect of injection of bile into a branch of the portal vein on the blood pressure and respiration. The vagi are divided.

the right side of the heart in great concentration and accordingly the action was more direct. Bile injected into a branch of the portal vein was first carried to the liver, where more even dilution occurred in the capillary bed, and on its return to the right side of the heart through the hepatic vein the concentration would not be so great. This explanation seems more reasonable because of the relatively slight difference in the toxicity of bile injected by the two routes.

The rise of the serum calcium at the conclusion of the experiments was a uniform result. The significance of this is not known. The average calcium content of nine specimens of mixed bile was 9.9 mg per hundred cubic centimeters. Accordingly, the elevated blood calcium could not be attributed to the calcium content of the injected material.

It is interesting to note that the cardiac arrhythmias occurred whether the vagi were intact or divided. Since the effect of atropine was not tested the conclusion cannot be drawn that the arrhythmias were entirely of myogenic origin from direct action on the heart.

CONCLUSIONS

1. The liver shows little, if any, tendency to become necrotic when injected into a branch of the portal vein.
2. There is a fairly uniform and rapid rise of serum bilirubin following the intravenous administration of bile.
3. Death may occur following the intravenous injection of bile before the van den Bergh reaction is appreciably elevated.
4. Division of the vagi does not diminish the activity of the vagus heart.

RELATION OF THE PYLORUS TO DURATION OF EXPERIMENTAL GASTRIC ULCER *

WALTER HUGHSON, M D

BALTIMORE

Efforts to produce chronic gastric or duodenal ulcers experimentally have met with indifferent success so far as any direct bearing on ulcers in the human stomach is concerned. Dogs, the experimental animals usually employed for this purpose, are notoriously immune to ulcerations of this nature, unless complex procedures are employed by which the normal physiology is so disturbed that conclusions cannot be drawn with any great accuracy. In recent years chronic experimental ulcers have been produced, notably by Dragstedt and Vaughn,¹ Hanrahan in an experimental study as yet unpublished, Mann² and his co-workers and Wolfer³. Any bearing that these reported experimental results may have on the subject would seem to be applicable more to the postoperative ulcer than to the primary one. Wolfer's experiments in which he produced ulcerations by exposing gastric mucosa over long periods of time to the roentgen ray, though of interest, apparently do not have any bearing on the general problem of ulcers. The production of experimental ulcer with streptococci, the selective theory of Rosenow,⁴ the use of isogastrotoxin and iso-enterotoxin in the production of ulcers by Myagawa⁵ et al and Nakashima's⁶ interesting corroboration of the "spasmogenic theory" need not be considered at this time.

In the course of experiments instituted to throw possible light on the etiology of primary ulcerations of the stomach and duodenum, incidental facts developed which seemed worthy of reporting. In 1916

* From the Surgical Hunterian Laboratory of the Johns Hopkins University Medical Department

1 Dragstedt L R, and Vaughn A M. Gastric Ulcer Studies, Arch Surg 8 791 (May) 1924

2 Mann, F C and Williamson, C S. Experimental Production of Peptic Ulcer, Ann Surg 77 409, 1923

3 Wolfer, J A. Chronic Ulcer of the Stomach, Its Experimental Production and Its Effect on Gastric Secretion and Motility, Ann Surg 84 89, 1926

4 Rosenow E C. Etiology of Spontaneous Ulcer of Stomach in Domestic Animals. J Infect Dis 32 384, 1923

5 Myagawa Y, Murai H and Terada M. Experimental Study of Cells of Mucous Membrane of Digestive Tract as Toxin or Irritant and Their Relation to Formation of Peptic Ulcer, Japan M World 3 136, 1923

6 Nakashima, Y. The Pathogenesis of Peptic Ulcer of the Stomach and Duodenum. Experimental Contributions on von Bergmann's Spasmogenic Theory. Ztschr f d ges exper Med 42 4 1925

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a total increase in the emptying time, but rather delay in emptying during any phase of the digestive cycle, or emptying at the expense of more vigorous muscular effort on the part of the stomach required to overcome the spastic contraction of the pyloric sphincter. The common roentgen-ray picture of a hyperactively contracting stomach is evidence of this fact, for peristaltic waves of the stomach itself cannot be increased in frequency and amplitude without a corresponding hyperactivity of the pylorus. Sphincter musculature can manifest hyperactivity in only one way—that is, by spasm.

The experiments detailed in the protocols were undertaken, therefore, to demonstrate what relation such pylorospasm might have on the development of ulcers in experimental animals. In previous experiments in which pylorospasm was produced, there had never been any indication of the development of ulcers, so that it was obviously impracticable to expect these ulcers to develop spontaneously. Also it seemed doubtful that an experimentally produced pylorospasm would persist long enough to make any particular differentiation possible. It appeared feasible, therefore, to occlude the pyloric opening partially, by almost any method and to study its effect on an ulcer made experimentally, controlling the observation on animals whose pylorus was intact. The familiar and easy method of injecting silver nitrate into the submucosa was chosen for the production of the ulcers. This proved not entirely satisfactory, so that later a small section of gastric mucosa was excised, about 1 cm in diameter, and the submucosa infiltrated with silver nitrate directly. At first an opening was made on the anterior wall of the stomach about 8 to 10 cm proximal to the pylorus, and the procedure I have described was carried out at a point about 2 cm proximal to the pylorus on the anterior wall. These ulcers all healed so rapidly that definite conclusions could not be drawn. Later the ulcer was made on the lesser curvature at a point about 2 cm proximal to the pylorus, and a striking difference was noted, as the ulcer developed a fair comparative degree of chronicity. The method of partially occluding the pylorus consisted of a procedure which might be termed a reverse Rammstedt operation. In other words, an incision was made on the anterior wall of the pylorus parallel to the circular fibers, the submucosa drawn out and a continuous silk stitch applied through a section of this layer for about 1 cm parallel to the long axis of the stomach and the incision through the muscle was closed in the opposite direction as in the Mikulicz operation. Animals were operated on in pairs the pylorus being occluded in one and not in the other while each had an ulcer or defect in the mucous membrane produced on the lesser curvature. These ulcers were either entirely removed at subsequent operation or else the animals were killed and the ulcers examined.

Contrary to expectation, in the first group of animals the ulcers in those whose pylorus had supposedly been decreased in size were found

almost completely healed when the sections were removed. Up to this time no fluoroscopic control of the stomach had been made. Following this observation, animals subsequently operated on were examined fluoroscopically on several occasions, following operation, and a rather unexpected fact was demonstrated. The emptying time of the animals whose pyloric ring had been divided and sutured was much shorter than those whose pylorus was intact, shorter in fact than the normal of three and four-tenths hours. After some consideration the explanation appeared fairly obvious. In those animals in which a partial occlusion of the pylorus had been attempted the continuity of the sphincter had been destroyed, and the suture of the submucosa had resulted actually in splinting the opening rather than occluding it.

Although the immediate effect may have been to delay emptying this was promptly overcome, and the result amounted to a permanent opening rather than one which went into phases of contraction and relaxation—a condition analogous to the rapid emptying found in annular tumors of the pyloric end of the stomach before the obstruction stage. Furthermore, in those animals whose pylorus had been left intact, a definite delay in the total emptying time of the stomach was noted. The explanation here was immediately clear, as the production of the experimental ulcer and the opening made in the anterior wall of the stomach produced peritoneal irritation and consequent hyperactivity or pylorospasm. Wolfe¹ made a similar observation in his animals with roentgen-ray ulcers, but attributes the effect—wrongly I believe—to “involvement of the local intrinsic mechanism by the ulcer placed close to the pylorus.” On the basis of these observations, a series of sixteen animals was used, half of which had what must now be spoken of as pyloric fixation and the other half an intact pylorus. These animals in pairs were killed at varying intervals of time after fluoroscopic controls had been made to confirm further the observations mentioned. This confirmation was obtained in every instance. The longest period of time elapsing between original operation and killing the animal was seven weeks. The remaining animals were killed at varying periods the shortest being three weeks. Typical protocols of such experiments follow.

PROTOCOL 1—Dec. 2, 1925. Dog, brown, female. Anesthetic, ether. Operation decreasing size of pylorus.

High right rectus incision. Pylorus exposed. Incision through musculature parallel to sphincter, exposing submucosa. Fine silk running suture through submucosa for distance of about 5 mm. This incision closed in opposite direction thus decreasing diameter of pylorus. Good condition. Closure with silk.

Jan. 26, 1926. Animal rather thin.

2:30 p. m. 300 cc. barium solution by stomach tube.

2:40. Fluoroscopic examination. Waves active but pylorus shows definite constriction. Just proximal to pylorus is pouch about 1 cm. in diameter which

is distended as waves advance toward pylorus Small amount of barium in intestine

4 25 Almost empty

March 8, 1926 Operation, laparotomy Excision of small area of mucous membrane on anterior surface proximal to pylorus Injection of 1 cc 10 per cent silver nitrate solution

April 1, 1926 Operation, laparotomy Stomach opened, but impossible to find even a scar indicating point at which mucous membrane was removed One area which seemed rather pale was removed for section

In this experiment with an emptying time of two hours in an animal whose pylorus had been splinted, practically complete healing of the ulcer took place in the brief period of three weeks

PROTOCOL 2—April 7, 1926 Dog, brown, male Anesthetic, ether

High right rectus incision Anterior wall of stomach opened 6 cm from pylorus Area of mucous membrane 1 cm in diameter removed on lesser curvature Injection of 1 cc 10 per cent silver nitrate into submucosa Stomach and abdomen closed

April 14, 1926 2 30 p m Fluoroscopic examination Three hundred centimeters barium solution by stomach tube

4 30 p m Still half full Marked delay in emptying Smaller crater can be seen on lesser curvature

Stomach examined through high right rectus incision Ulcer 1 cm in diameter on lesser curvature Examined through opening on posterior wall of stomach Wound closed

May 3, 1926 Animal dead of distemper Autopsy Marked ulceration on lesser curvature Some crater formation with slough Little evidence of healing

This ulcer is shown in figure 5 With no splinting of the pylorus a delay in the emptying time was observed, and the experimental ulcer showed little indication of healing at the end of approximately four weeks

The results were remarkably uniform in their general outcome Microscopic sections of the ulcers were examined in the majority of cases, but added nothing particular to the information obtained from the gross appearance The ulcers cannot in any sense be compared to the chronic ulcer in the human stomach, but simply represent a defect in the mucous membrane with a slough developing in the submucosa, with some crater formation and a chronic inflammatory reaction in the immediate surrounding tissues Healing takes place by a separation of the slough in the submucosa, cicatrization of the defect thus made and covering over of the area with mucous membrane

Figure 1 represents an ulcer approximately 1 month old in an animal whose pylorus had been splinted and which had a normal emptying time It can be seen that this ulcer is practically healed, although there is marked scarring and thickening of the wall of the stomach evident in the lateral view Figure 2 represents one of the earlier experiments in which the ulceration was made on the anterior wall of the stomach

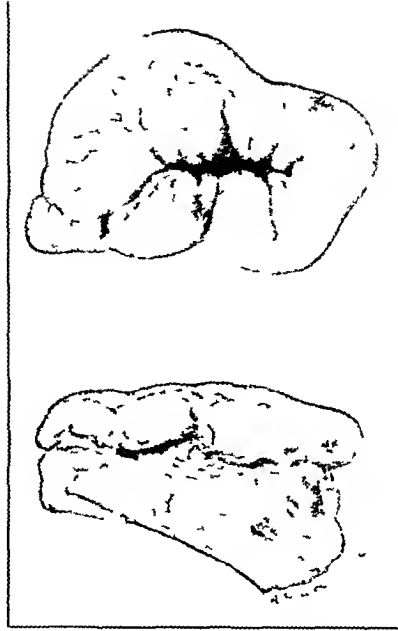


Fig 1—Ulcer produced by injection of silver nitrate through the wall of the stomach, duration, one month Pylorus splinted Upper view shows scarring in the mucous membrane, lower view thickening of the submucosa

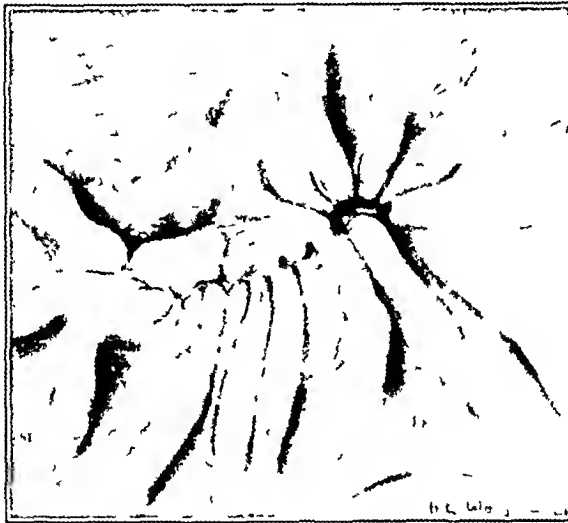


Fig 2—Ulcer on anterior wall of the stomach next to the suture line Ulcer practically healed in three weeks Pylorus splinted



Fig 3—Ulcer on the lesser curvature in animal with intact pylorus

This ulcer had practically healed in three weeks. The pylorus was also fixed in this animal. Figure 3 is the ulcer resulting from the experimental procedure carried out on the lesser curvature in an animal whose pylorus had remained intact. Three weeks had elapsed between the operation and killing the dog. It will be noted that the defect in the mucous membrane is here of considerable size, although the slough in the submucosa is not so apparent. The control in this experiment died of distemper one week following the original operation. Figures 4 and 5 represent experiment and control, figure 4 showing the appearance of the ulcer in an animal whose pylorus had been fixed. The defect in the mucous membrane is still evident, but the slough in the submucosa has healed over almost entirely. The relation of the ulcer in figure 5 to the pyloric sphincter is evident, the duodenal mucous membrane showing clearly to the left of the picture. Here a large slough, about 1 cm in diameter, is still apparent, this tissue being necrotic and showing marked inflammatory reaction. There has been no attempt on the part of the mucous membrane to cover the defect. Figure 6 shows the experiment and control again. The control observation is shown at the top with the ulceration practically healed and the mucous membrane markedly puckered. The effect of splinting the pylorus is seen at the left. In the lower figure the ulcer is still active, in the middle there is a definite slough, and the mucous membrane has made but little progress in the process of covering the defect. These animals both remained alive and well for seven weeks following the original operation.

COMMENT

From the data obtained in these experiments and the description of the drawings, certain facts seem fairly evident. Experimentally produced defects in the gastric mucous membrane with an injection of 10 per cent silver nitrate into the underlying submucosa require a longer time to heal, if the pylorus is intact, than those produced in a stomach with a splinted pylorus. In the foregoing discussion these defects have been referred to as ulcerations. The propriety of such an appellation is of course, dubious, but doubtless it is as nearly correct as the term used in connection with the intravenous injection of streptococci or in Dragstedt and Vaughn's experiments in which mucous membrane was excised and silk stitches were left hanging from the submucosa. Too free interpretation of experimental results in terms of human pathology is a pitfall which should be carefully avoided. The very difficulty experienced by all investigators in producing experimental ulcers in dogs is evidence enough of this danger.

The reflex mechanism of the pyloric sphincter in dogs does, however, behave in a manner similar to that seen daily in clinical medicine and surgery. As has been stated hyperactive muscular contraction of



Fig 4—Ulcer in animal with fixed pylorus Slough had separated, and defect had almost healed in submucosa, one month's duration



Fig 5—Companion to figure 4 Animal with intact pylorus Extensive slough in submucosa, one month's duration Pyloric ring and duodenal mucous membrane seen to left of illustration

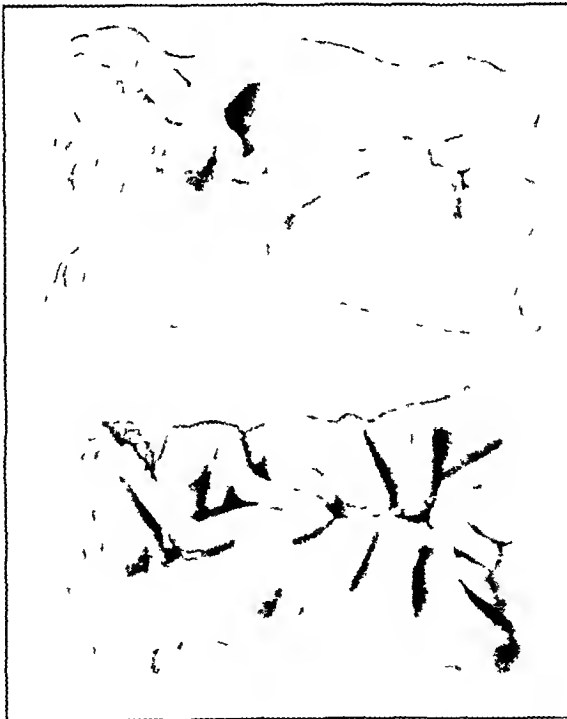


Fig 6—Experiment and control seven weeks duration Upper view of specimen from animal with fixed pylorus This can be seen to the left of the picture Ulcer on lesser curvature practically healed Lower view of the intact pylorus with ulcer still present Crater-like defect in submucosa

the stomach is undoubtedly responsible for a large number of the symptoms of all abdominal diseases. This hyperactivity must manifest itself by pyloric contraction, and a delay in emptying of the stomach, either total or relative, results. The establishment of proper drainage of the stomach in the presence of ulceration, whether benign or malignant, results always, no matter what the method employed, in a prompt subsidence of the organic reaction and in many instances in actual cure of the ulceration. This being true, it is entirely reasonable to suppose that the opposite condition, delayed emptying or poor drainage, should be largely responsible at least for the growth of the ulcer. Reference to its part in the actual etiology is purposely avoided at this time. The experimental observations outlined herewith amply confirm this opinion, for evidence has been brought forward to show that experimental ulcers with an intact pylorus cause delay in emptying. When the emptying is hastened, and this was not at the expense of greater muscular effort but simply by splinting the pyloric sphincter, the ulcers healed in a minimum length of time. Chemical studies have not been made, for if there were changes in the gastric juice, this also would be caused by the delayed emptying. The extremely high acid values found in complete pyloric obstruction is the most striking example of this particular cause and effect.

It is believed, therefore, that the relationship between duration and possibly severity of ulceration of the stomach and the emptying of the stomach has been demonstrated experimentally. Furthermore, presumptive evidence is advanced to indicate that this factor of emptying plays an extremely important rôle in the whole life history of the ulcer. Though possibly nothing in the way of actually new information is brought forth by this demonstration, nevertheless one of the many vaguely appreciated clinical concepts has been given adequate experimental support.

CONCLUSIONS

- 1 Experimentally produced ulcers on the lesser curvature of the dog's stomach result in a delayed emptying of the stomach in the presence of an intact pylorus.

- 2 Splinting of the pylorus in these experimental animals obviates this delayed emptying.

- 3 In the animals in which delay is demonstrated, ulcerations remain active at least twice as long as in the group in which the emptying is more rapid.

- 4 This delay is due to reflex contraction of the pyloric sphincter.

COALITION OF THE CALCANEUS AND THE NAVICULAR

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Rigid flatfoot is generally considered to be the result of prolonged eversion and abduction, unrelieved by treatment. A failure of proper balance of the foot because of congenital or acquired weakness is considered the primary fault. The mechanism of the development of the alteration in relationship to the tarsal bones is dependent on the faulty position of the foot, which throws excessive and prolonged strain on ligamentous structures. The ligaments are not physiologically capable of resisting prolonged strain, and give way, allowing the tarsal bones to rotate into the typical deformity of flatfoot. The altered position of the tarsal bones and their articulations tends to produce a rigid foot.

Although the rigid foot is less mobile than the normal one, it is frequently asymptomatic. In some cases, however, the foot remains painful, and the rigidity is greatly exaggerated by muscle spasm chiefly of the peroneal group. This condition produces more or less severe disability, which can frequently be relieved by appropriate treatment by standard methods.

At the University Hospital there have been a few obstinate cases in which cure has not resulted. The treatment was based on the accepted doctrine that the mechanism of the development of the rigid flatfoot with peroneal spasm was dependent on a primary defect in the soft tissue with a secondary alteration in the skeleton of the foot. This assumption proved fallacious, for there is another mechanism for the development of the rigid flatfoot, which is not generally considered. A review of the resistant cases, in which the patient did not improve under the standard therapy, demonstrated a malformation or deformity of the calcaneus or navicular, which in this group undoubtedly is the primary cause for the development of a rigid foot. In these cases, the rigid foot was not produced by a primary failure of the soft tissue with a secondary change in bone, but rather by a primary abnormality in the growth of the bone with secondary change in the soft tissue.

My first conception of the possibility that rigid flatfoot results from a congenital abnormal formation of the bone was obtained from an article by Slomann,¹ of Copenhagen. Slomann was apparently the first to recognize the condition clinically. He reported five cases in an article entitled "On Coalitio Calcaneo-Navicularis" which appeared in 1921.

1. Slomann. On Coalitio Calcaneo-Navicularis. *J. Orthop. Surg.* 3: 58, 1921.

In his article, he gives Holl, of Vienna, credit for first observing the coalition in two cases examined in the anatomic laboratory

The knowledge of the etiology of the bony fusion between the calcaneus and navicular is derived from a study by W Pfitzner, of Strassburg Pfitzner believed the coalition must arise from abnormal



Fig 1 (case 2) —Coalition of the calcaneus and navicular complete An excellent illustration of complete fusion with a bony bridge



Fig 2 (case 2) —The normal foot of the same patient, showing no roentgenologic evidence of a calcaneus secundarius

development of the tarsalia He studied skeletons of 840 feet, and found the development of a tarsal bone, the calcaneus secundarius, in nine, or 1 per cent of the cases Slomann quotes Pfitzner freely in describing the development of the calcaneus secundarius into the various stages of coalition

At that point of the tarsus skeleton where the processus anterior calcanei, the cuboideum, the navicular and the caput tali meet, without, however, all coming into direct touch, is to be found, with careful dissection in a certain number of cases, a little bone of irregular shape, the so-called calcaneus secundarius. This tarsale appears symmetrically in that when present it always appears in both feet. Its size and independence may differ greatly in the two feet. In the more developed tarsale four surfaces facing the four bones mentioned can be made out. The surfaces facing the talus and cuboideum are

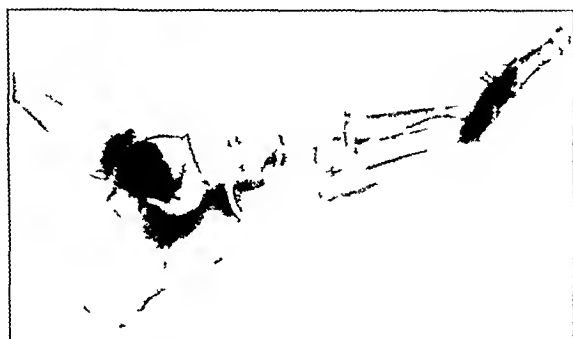


Fig 3 (case 4) —The fusion of the calcaneus secundarius to the calcaneus in the right foot is shown here. The development is not large, but it produced definite symptoms. The bilateral appearance of the tarsale is shown in this case and also the tendency toward an asymmetrical development.



Fig 4 (case 6) —Fusion of the calcaneus secundarius to the navicular with almost complete coalition of the calcaneus to the navicular. The coalition is probably complete, with the clear area between the two processes a cartilaginous band.

articular surfaces while those facing the processus anterior calcanei and the navicular are attached to these bones by a fibrous tissue. If the calcaneus secundarius is strongly developed, it in this way forms a bridge between the calcaneus and navicular, and if now it follows the tendency of the process of the tarsalia to fuse to the neighboring bones, it may show itself either, as is most usual, as a protuberance on the calcaneus (fig 3) or as a protuberance on the navicular (fig 4), or finally, if it attaches itself closely to both, as a calcaneo navicular (figs 5, 6, 7 and 8).

"Pfitzner has described 15 cases himself of such coalition, and has collected 38 from the literature" Holl and Slomann emphasized the presence of the abnormality associated with flatfoot Pfitzner denies the necessary association of the coalition with flatfoot In the group of cases in the University Hospital rigid flatfoot with peroneal spasm

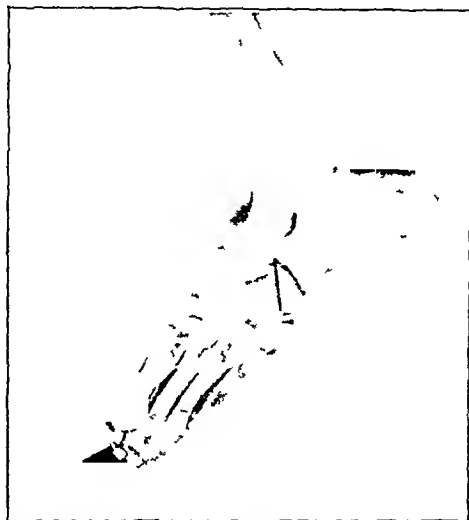


Figure 5



Figure 6

Figs 5 and 6 (case 1) —Fusion of the calcaneus secundarius to the anterior medial end of the calcaneus with practically complete coalition to the navicular The clear space is not an articulation, but cartilaginous tissue

was constantly present Slomann believes "the deformity to be due to the manner in which the anterior component of the body weight, acting downward and forward through the corpus tali, is transmitted through the caput tali to the navicular and then stopped up by the coalition, is

transferred directly to the foremost and innermost point of the calcaneus (instead of, as in normal conditions, being transmitted from the navicular forward through the cuneiforme I to the metatarsale I), which rotates the calcaneus inward and lays its foremost part down flat against the ground." It is also quite possible that either the complete osseous union, or the union of the calcaneus secundarius to the navicular or calcaneus may alter the relation of the tarsus during the growth of the skeleton of the foot. The latter theory is supported some-



Fig 7 (case 5)—Roentgenogram made from the oblique position shows the solid bony bridge connecting the calcaneus and navicular, a true coalition

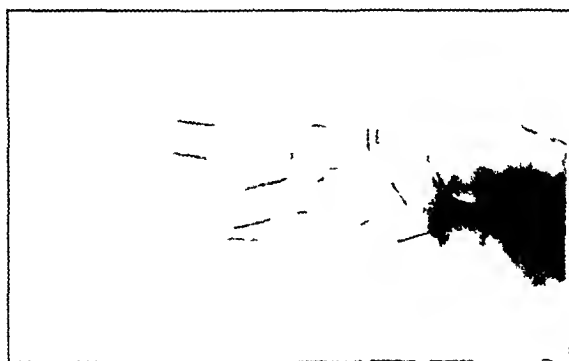


Fig 8 (case 5)—Roentgenogram made in the anterior-posterior position shows the definite coalition of the calcaneus and navicular

what by the marked uniformity of appearance of symptoms at the age of puberty

During the past year I have seen five cases which showed various stages in the fusion of the calcaneus secundarius from the stage of fusion to the anterior medial end of the calcaneus, to the formation of a complete bony bridge between the calcaneus and navicular. In all of these cases there was a severe disability of the affected foot with pain and discomfort when it was used. The rigidity of the foot was an

proportion to the amount of fusion, but in all cases lateral mobility was definitely limited. Motion of the ankle joint proper was unaffected in all cases. Peroneal spasm was present in all cases.

In only one case did the patient respond favorably to the standard methods of treatment used for pronated rigid foot with peroneal spasm. It is not known whether this patient obtained complete relief, as he



Fig 9 (case 5) —Postoperative roentgenogram made from oblique position showing resection of bony bridge. The markedly increased separation of the cuboid from the navicular is now obvious, as is also the relation of the external cuneiform to the bony bridge.

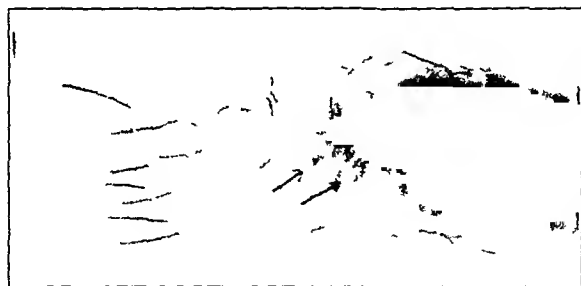


Fig 10 (case 5) —Postoperative roentgenogram from anterior-posterior position demonstrates removal of bony bridge and illustrates its relation to the tarsal bones.

returned to the clinic but once after the treatment was instituted. The other four patients showed no improvement. In two cases lengthening of the peroneal tendons in addition to repeated manipulations to correct the deformity followed by retention in bivalved plaster casts, and by the usual postoperative massage exercises and other forms of physiotherapy failed to give relief. Two patients who showed a definite

bony bridge between the calcaneus and the navicular were treated by operation planned to eradicate the primary deformity of the bone. It is too early in either of these cases to state the result of this form of therapy, but present evidence points toward satisfactory results in both. The procedures employed with the results are discussed in the abstract of the case (figs 9, 10 and 11).

I have an additional case of partial coalition of the calcaneus and the navicular, which was seen in the clinic some years ago. A lantern



Fig 11 (case 2)—Foot of patient in case 2 following resection of bony bridge and arthrodesis of the subastragaloid and astragaloscaphoid joints



Fig 12 (case 5)—Roentgenogram made from the lateral position gives little idea of the coalition. The malformation of the anteromedial end of the calcaneus is obvious. Note the bony overgrowth on the talus seen commonly in this condition.

slide of the roentgenogram was preserved by Van Zwalenberg is an interesting and rare case. I do not have the history of the patient, but the lantern slide shows the typical deformity.

The abnormal development of bone caused by the tarsal coalition secundarius is sufficiently frequent to warrant more general recognition. My own failure to recognize the deformity in spite of a search for it since 1920 I believe to be due to improper projection of the roentgen

ray The usual lateral and anteroposterior roentgenogram shows the deformity poorly, as is illustrated in case 5 (fig 12) An oblique position, as demonstrated in the illustrations, shows the abnormality well With this roentgen-ray technic, the coalition will be observed frequently in a large clinic



Fig 13 (case 5) — 1 indicates the bony bridge attached to the calcaneus and navicular The relation of the bridge of bone to the cuboid, external cuneiform and the caput tali is well shown The bony overgrowth on the caput tali is seen on the dorsolateral surface just back of the articulation The posterior calcaneotragaloid joint is seen just above Allis clamp The dotted line represents the segment of bone removed B indicates the resected bony bridge, C, drawing made after removal of bridge

I do not believe that the usual procedures employed for rigid flat-foot of the primary soft tissue type will be of benefit in the majority of these cases.

I do not insist on my own operative methods in the treatment of these patients since my experience and material are too meager and I have seen no reference to operation previously in this type of case. I feel, however, that operation in the conditions that resist conservative treatment is indicated. I believe that in the complete fusion type it is possible that a mobile foot, functionally satisfactory, can be obtained by resection of the coalition (fig. 13), if the operation is undertaken early after the onset of symptoms. If considerable delay has occurred, it is probable that traumatic changes in the subastragaloid and calcaneonavicular joints have developed which will require arthrodeseis of the affected foot for relief of the symptoms.

CONCLUSIONS

- 1 Coalition of the calcaneus and the navicular, partial or complete, is a possible cause of rigid flatfoot, which should be differentiated from the usual type.

- 2 The usual routine roentgenogram does not sufficiently demonstrate the deformity. The direction of the ray should be oblique to the foot. The abnormal formation of the bone is then clearly shown.

- 3 There is frequently bony overgrowth on the caput tali associated with coalition that may lead to an erroneous diagnosis of arthritis as the cause of the disability.

- 4 The appearance of symptoms at the age of puberty is a striking factor in the clinically reported cases.

- 5 The failure of the customary forms of treatment for rigid flatfoot with peroneal spasm in this type of case suggests the need of more radical therapy. Lengthening of the peroneal group has proved to be of no value in my cases. Resection of the bony bridge may give a mobile functional foot. Arthrodeseis of the subastragaloid, calcaneonavicular and calcaneocuboid joints may be necessary in further advanced cases.

REPORT OF CASES

CASE 1.—R. V., a boy, aged 13, entered the hospital in September, 1926, with pain and deformity of the right foot. The pain had not been marked and was present only after prolonged use. The deformity was marked and for this reason the parents brought the child to the clinic.

Examination showed that the right leg was three-fourths of an inch (1.27 cm.) short; there was three-fourths of an inch atrophy of the right tibia; one inch (2.54 cm.) atrophy of the calf. There was also a slight valgus deformity with marked pronation with definite peroneal spasm.

Thomas heels, an anterior wedge to the sole of the shoe and splints were prescribed.

This patient showed a definite coalition of the calcaneonavicular joint and operation was discussed with the father, if the conservative form of therapy proved unsuccessful.

The patient returned to the clinic on November 5, and showed some improvement. He has not been seen since.

CASE 2—E O, age 13, entered the hospital on March 30, 1925, with a stiff, painful ankle and foot. The onset was gradual, the summer before, with no previous history of injury. There was pain if the foot was overworked, marked limitation to lateral motion and pain on walking on rough ground, but no limp or pain after walking a short time.

Examination showed a marked limitation of the subastragaloid joint, limited mediotarsal joint, free motion of the ankle joint, marked pronation with valgus deformity and peroneal spasm.

An attempt at conservative therapy was employed, with no relief.

On Aug 27, 1926, an operation was performed through an anteriolateral incision. A well defined bridge projected from the anteromedial portion of the neck of the os calcis and had fused as one piece with the under surface of the scaphoid. The anterior and posterior facets of the astragalus were surrounded by and included in a wall of firm fibrous tissue. There was a medial rotation of the os calcis on its long axis. The bony bridge was resected. Osteochondral excision of the articular surface of the astragalus and scaphoid and the astragalocalcaneal joints was performed. The patient's foot was placed in a plaster cast in a corrected position, and the wound healed primarily.

The patient returned to the clinic on Dec 10, 1926. Two months after the operation there was a recurrence of the pronation deformity of the foot and a marked peroneal spasm. Manipulation under anesthesia corrected the deformity. The foot now shows good position with slight valgus. The arthrodesis is apparently solid. The patient was fitted with an inside upright, an outside T-strap and a night mold, and was told to return in three months.

This patient had a marked bony coalition of the calcaneus and navicular with a development of a periartthritis about the subastragaloid articulations. It was deemed necessary to perform the arthrodesis because of changes in the joint.

CASE 3—E S, a Finnish girl, aged 17, entered the hospital on July 14, 1925, complaining of pain in the right foot, with difficulty in walking. The onset had occurred five years before, following a twisting of her ankle. She had had mild symptoms since this injury, which had increased recently. There was dull pain, only occasionally sharp, worse in the morning and in hot weather (fig 14).

Clinical examination showed a spastic, rigid flatfoot in marked pronation, active and passive attempts at inversion were impossible. There were tenderness over the scaphoid and marked peroneal spasm. The condition was considered a rigid flatfoot with peroneal spasm secondary to arthritic changes in the tarsal bones.

On Sept 8, 1925, the patient had an operation to lengthen the peroneal tendons, followed by wrenching of the foot under ethylene anesthesia, and the application of a plaster cast to maintain varus cavus correction. The cast was bivalved. Baking and exercises were instituted after healing of the operative wound. A correction of the deformity was not obtained by this procedure, so on October 14 another manipulation was attempted. The patient was apparently somewhat relieved by this treatment, and was discharged wearing Thomas heels and stiff shank shoes, to continue her exercises.

She returned on Aug 13, 1926, with a recurrence of the deformity and symptoms. Manipulation under anesthesia was again performed. Visible breaking up of adhesions and apparently a good correction of the deformity was obtained.

The patient has not been seen in the clinic since this manipulation.

The roentgenograms of this patient's foot show a very definite calcaneus secundarius with a fusion to the anterior medial end of the calcaneus. I believe a subastragaloid arthrodesis will be necessary in this case.



Fig 14 (case 3)—Partial coalition. Fusion of the calcaneus secundarius to the anterior medial end of the calcaneus. The long projection and malformation of this portion of the calcaneus is clearly shown. The spur formation on the caput tali is frequently seen in these cases. There is no contact with the navicular.



Fig 15 (case 4)—The process in this case is much more developed and the flatfoot more marked. Note the tendency for spur formation on the caput tali and the navicular.

CASE 4—R. M., a girl aged 15, entered the hospital on Oct. 28, 1925, complaining of painful feet. The patient was well developed and otherwise healthy, with a definite hump. She said that she had always had trouble with her feet and was unable to walk any distance without pain. Standing for any length of time was painful.

Examination showed a marked pes planus deformity with definite peroneal spasm.

The peroneal tendons were lengthened in both feet in September, 1925. Plaster casts were bivalved so that physiotherapeutic measures could be employed. Casts were removed on November 29, and Thomas heels and exercises were prescribed.

The patient returned on May 17, 1926, with some relief from pain, but still having symptoms. On June 11, 1926, both feet were manipulated under anesthesia with an unsatisfactory correction, and on July 17, 1926, a second manipulation was performed.

This patient has a definite fusion of the calcaneus secundarius to the anterior medial surface of the calcaneus. An arthrodesis of the subastragaloid joint will doubtless be necessary before she obtains relief from symptoms (fig 15).

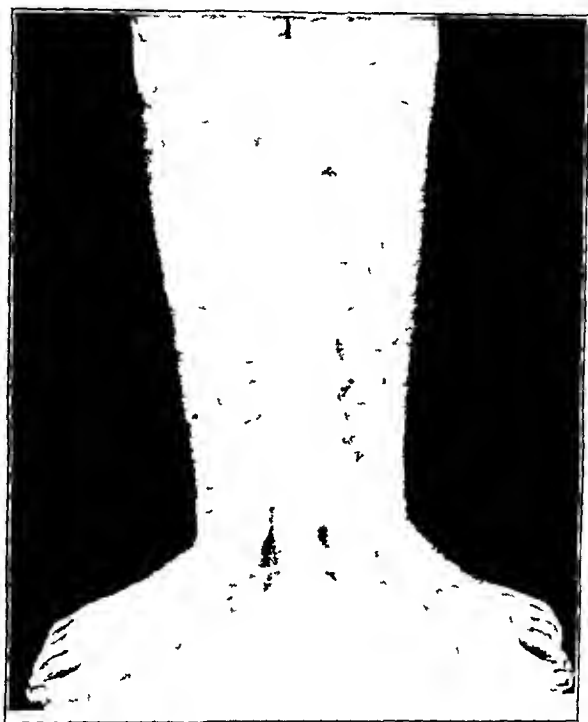


Fig 16 (case 5)—Photograph made before operation. The pronation of the feet, more marked in the left, is obvious.

CASE 5—A McK, an American girl, age 13, entered the hospital on Aug 12, 1925, with pain and swelling of the right knee (figs 16 and 17). She gave a history of pain in the left ankle a year before. This gradually disappeared, and the right knee later became involved. There was a definite synovitis of the knee with increased fluid and slightly thickened synovial tissue, but with little loss of motion.

Two months after entering the hospital the patient complained of pain in the left ankle and difficulty in walking. The left foot was held in marked pronation. Active and passive supination was impossible because of marked rigidity and peroneal spasm. There was a definite atrophy of the calf muscles.

On Nov 12, 1926, an attempt was made to correct the deformity by manipulation under anesthesia. Inversion could not be obtained, but a cast was applied and bivalved so that physiotherapy could be instituted.

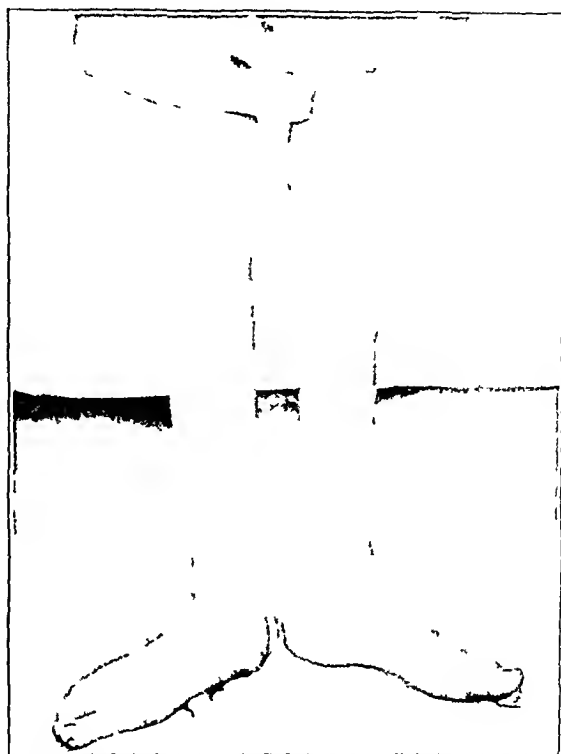


Fig 17 (case 5) —Postoperative photograph of left foot, demonstrates increased varus and correction of pronation

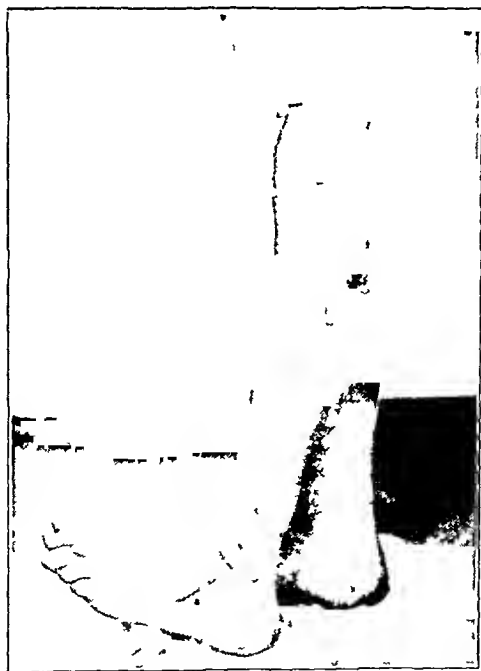


Fig 18 (case 5) —Postoperative photograph demonstrates approach employed and the absence of peroneal spasm Active inversion is possible

Two months later there was no evidence of any improvement in the condition, and a roentgenogram demonstrated evidence of the bony bridge between the anterior processes of the calcaneus and the navicular.

An operation was performed on Jan 17, 1927. An anteriolateral incision was used, exposing a bony bridge attached to the anteromedial surface of the os calcis into the lateral inferior portion of the navicular. There was a curious cauliflower-like bony overgrowth at the border of the cartilage on the dorso-lateral surface of the head of the talus. The external cuneiform and the cuboid articulated with the bony bridge. The interval between the anterior end of the calcaneus and the navicular was greatly increased. The subastragaloid joint was normal in appearance. The bony bridge was removed from the navicular and the calcaneus. Following its removal, the foot was perfectly mobile, and complete inversion could be obtained. In view of the normal appearance of the articulations no attempt was made to perform arthrodesis on the subastragaloid joint. The wound was closed in layers, and a plaster cast was applied with the foot in marked inversion and supination.

The patient had an uneventful convalescence. The wound healed by primary union. The patient could hold the foot in inversion actively ten days following the operation, and could stand with the foot well corrected. The patient was discharged with a bivalved plaster to wear at night, and with an outside upright and inside T-strap attached to a shoe that had a Thomas heel and a wedge on the inner sole.

This patient had a definite bony bridge between the calcaneus and navicular, which was the cause of the rigidity of the foot. It is too early to tell whether the correction of the deformity will be permanent, but I anticipate success.

CASE 6—R was seen in the University Hospital some years ago, and I can find no record of the history. I have only a lantern slide which was saved by Van Zvalenberg as demonstrating a rare and interesting condition.

DEPOSITION OF CALCIUM SALTS IN AREAS OF CALCIFICATION

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In former papers I have reviewed evidence as to the manner of the transport of calcium salts in the blood stream and their deposition in bone and in calcified areas. The deposition of calcium in bone is in an extremely fine form and in such a manner that from appearances alone it might be interpreted according to the bias of the observer either as a secretory phenomenon of the osteoblasts and bone cells or as a precipitation phenomenon. Correlated with physiologic evidence, however, the balance of proof is in favor of the secretory view. The object of this investigation, was to learn whether such was also the case in areas of calcification. In this paper I shall review the information I have obtained by the examination and study of various calcified areas, and shall discuss the conclusions to be made from the facts presented.

MATERIAL

All of the material used for this investigation was human and consisted of sections of arteries varying in size from that of areas of the wall of the aorta to that of vessels such as the radial and ulnar arteries. Calcified areas of choroid plexuses of the brain, also parts of the pineal gland and the thyroid gland were investigated.

TECHNIC

In all cases the purpose was to examine undisturbed calcium deposits, and so the specimens were only rarely decalcified, and then only for examination in conjunction with similar ones in which the calcified areas were left intact. It is possible to cut areas of calcification if they are not too heavy, and sections from 10 to 20 microns thick were obtained. Of course, the sections tend to break up and are not perfect, but even the fracturing of the calcified areas gives valuable information at times. It is well to reserve an old microtome knife for this work alone, as the edge is necessarily spoiled.

The great majority of specimens were preserved in solutions of formaldehyde or of formaldehyde-saline. Hematoxylin, eosin and also Mallory's triple stain were usually employed. Methylene blue, Schmorl's stain and others were used occasionally. By fixing precipitates of calcium carbonate and calcium phosphate to cover-glasses and subjecting them to all of the processes of embedding and staining, I have previously shown that no alteration was occasioned in these precipitates, so it may be assumed that any masses of calcium deposits seen in any sections are in the same form after the preparation of the sections as they were previous to the manipulations.

In every case, sections of a specimen were mounted clear and unstained, in addition to those stained in various ways. By this means it was possible to make a good dark-field examination of many specimens in addition to the usual light-field examination.

EXAMINATION OF CALCIFIED AREAS

Calcification may be divided roughly into two kinds, physiologic and pathologic. Physiologic calcification is the normal process which occurs in developing bones just previous to the beginning of ossification. It occurs in a living, healthy tissue. Pathologic calcification occurs in tissues which normally do not contain deposits of this kind, and it is usually preceded by some injurious process in the tissues which leaves them dead or in a damaged condition. It may also occur in old fibrous tissue. The two processes will be studied separately, pathologic calcification being investigated here, and the results of the physiologic process being published in a future paper.

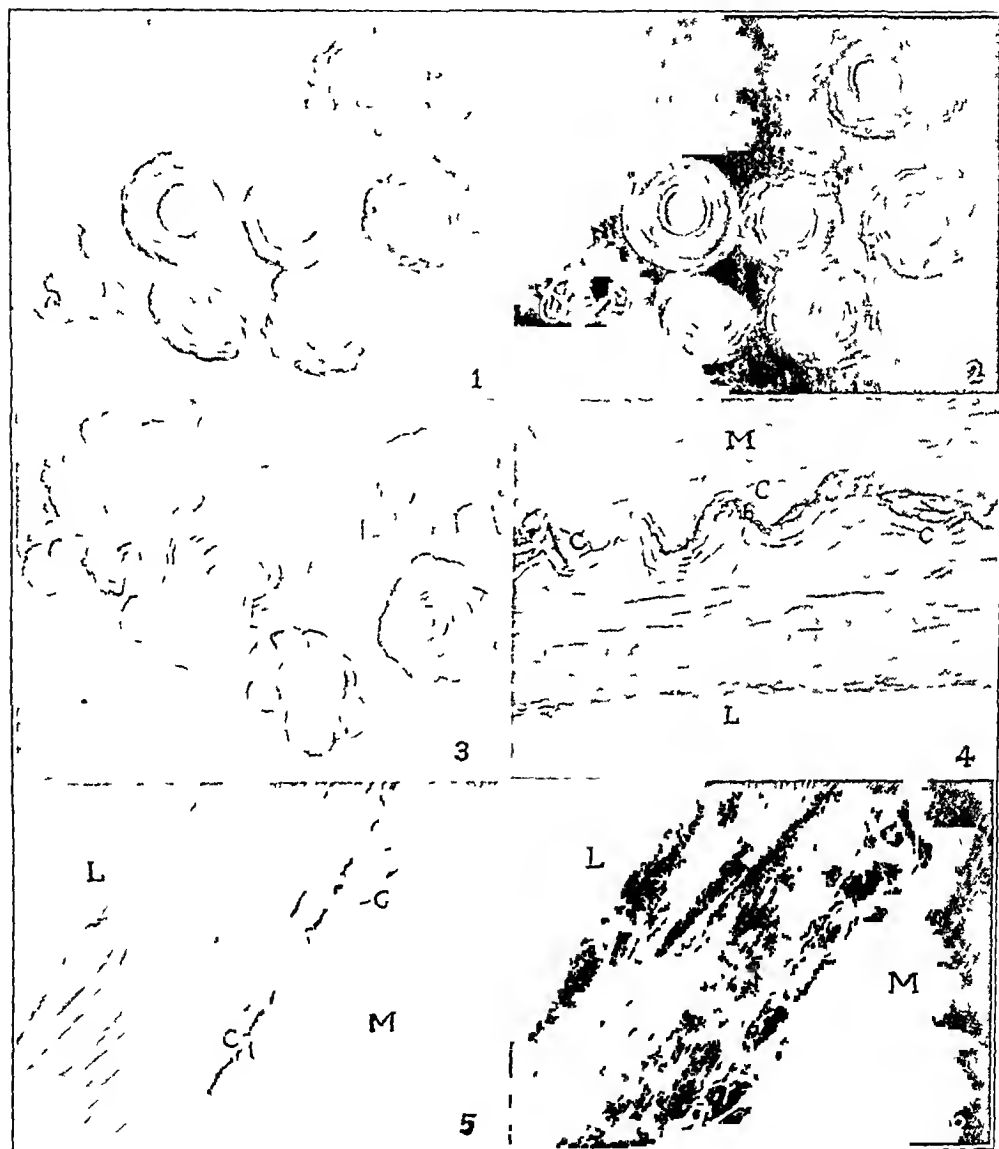
PATHOLOGIC CALCIFICATIONS

Pineal Gland—Longitudinal sections, 10 microns thick, were made of a pineal gland. It was thickly set in its distal portion with small hard masses which gave a gritty sensation when cut. Microscopically examined, these masses were very noticeable, as they were intensely stained with hematoxylin (fig 7), and it was found that sections had to be stained lightly in order to show any detail. The deposits varied in size from minute spherical bodies, 1 micron in diameter up to single bodies from 8 to 10 microns in diameter. Bodies of a larger size ranging up to 150 microns were seen, but these clearly indicated that they originated from a fusion of several smaller masses. In unstained sections (fig 3) the calcified areas appeared as glassy, crystalline masses. On close examination many of the areas showed a shading in their interior which was much darker in the center, while some, which exhibited concentric rings, gave indications of being laid down in layers.

The appearance of the deposit was strikingly similar to that of spherules of calcium carbonate and phosphate precipitated in a colloidal medium, as shown by the dark center, concentric layers, clear glassy appearance, round spherical form and a tendency toward fusion into large masses.

In some places a definite fibrous wall seemed to surround the deposits completely, but in other cases the glandular tissue was in direct contact with the deposit. No cellular structure was in any way visible in these calcified areas. Specimens were decalcified, and when this was done only the colloidal matrix remained in which the calcium salts were deposited. The matrix appeared homogeneous and reproduced accurately, like a mold, all of the features of the calcareous areas, the

PLATE 1



EXPLANATION OF PLATE 1

These six figures are from drawings by Miss M. T. Wishart, artist of the Faculty of Medicine, University of Toronto. The drawings are from camera lucida tracings.

Fig. 1—Deposits of calcium in the form of spherites in the choroid plexus of the descending horn of the lateral ventricle. The specimen was unstained and the fine tissue of the plexus was invisible with ordinary lighting, $\times 80$.

Fig. 2—Same as figure 1, seen with dark-field illumination. The tissue of the plexus is faintly indicated especially in the lower part of the figure, $\times 80$.

Fig. 3—Unstained specimens of pineal gland, glandular tissue invisible, calcium spherites shown with indications of their formation by fusion of smaller bodies, $\times 80$.

Fig. 4—Section of wall of brachial artery unstained, showing commencing calcification just internal to muscular layer, calcium in masses of granules and irregular fused lumps. In this figure and in figures 5 and 6, *L* indicates lumen of artery, *M*, muscular layer, *C* deposits of calcium, $\times 160$.

Fig. 5—Section of wall of femoral artery unstained, showing calcification just internal to muscular layer. $\times 120$.

Fig. 6—Same as figure 5 with dark-field illumination, $\times 80$.

indications of concentric layers and the lines of fusion of contiguous deposits to form larger masses being clearly visible

Dark-field illumination of unstained sections showed that the calcified areas were clear and glassy and crystalline in appearance, while the surrounding tissues had only a fraction of the brightness shown by the deposit. Examination with a polarizer showed that some of the deposit was doubly refracting and therefore definitely crystalline in nature.

It may be taken as proved that the masses in this pineal gland were a deposit of calcium because of the following facts: (1) the deposit had an intense affinity for hematoxylin, (2) the appearance of the deposit resembled that of calcium salts precipitated in a colloidal medium, (3) decalcification occurred under appropriate treatment leaving the organic matrix in which the deposit occurred as an excellent replica, which, however, showed different staining reactions, (4) the masses were of all sizes, and the large ones showed many evidences of fusion and fracture in layers and along lines indicating these fusions, (5) some of the deposits showed the behavior of a crystal to polarized light.

The composition of the mass was demonstrated by microchemical means. By the addition of strong acids, such as hydrochloric, effervescence was seen on the unstained sections, showing the presence of carbonates. A dense amount of phosphate was demonstrable by the silver nitrate reaction. By means of the prussian blue reaction, iron was proved to be present in the crystals, but not in such quantity as to be the main part of the mass. Eaves and others have shown iron to be commonly present in calcified areas in the central nervous system, and it is certainly present in this case in a fair amount.

That the process of deposition was by simple precipitation is evidenced also by the facts already enumerated, which are identical with the observations in experimental precipitation in colloidal mediums. This is further proved by the absence of any cellular content in the deposits, such as would be capable of laying down calcium by its secretory activities. In some areas, the pineal cells appeared to be in direct contact with the calcified areas, but it is inconceivable that they could have had any power in forming the area.

Similar deposits of calcium are described by Eaves, who shows illustrations for masses found within the brain which are much like mine.

Choroid Plexuses—Sections of choroid plexus were examined from the roof of the third ventricle of the human brain, and also from the body and descending horn of the lateral ventricle. These plexuses contained numerous fine nodules which appeared calcareous, and on section were proved to be so. The areas of deposit stained intensely with hematoxylin, many showed concentric layers, examples of fusion were common, and great variation in size occurred, but there were no masses of such size as those seen in the pineal gland.

Mallory's stain colored the calcified areas blue, and after decalcification, the organic matrix of many of these areas appeared orange yellow. Dark-field illumination of unstained sections (fig 2) showed the deposits as bright, shining, crystalline areas standing out sharply. When these areas were tested with polarized light they were found to be doubly refracting.

The calcium in the choroid plexus in the descending horn of the lateral ventricle appeared as irregular shaped masses (fig 10) of closely packed granules, the edges of the masses being wavy and irregular in contour and showing distinctly the granular character. Many fine granules were found scattered about where some of these masses had been broken in cutting the sections, and it is certain that these were not stain deposits, as they were exactly similar to the granules seen in the clumped masses of precipitation, and they were not found in any other part of the sections except in the broken calcified areas.

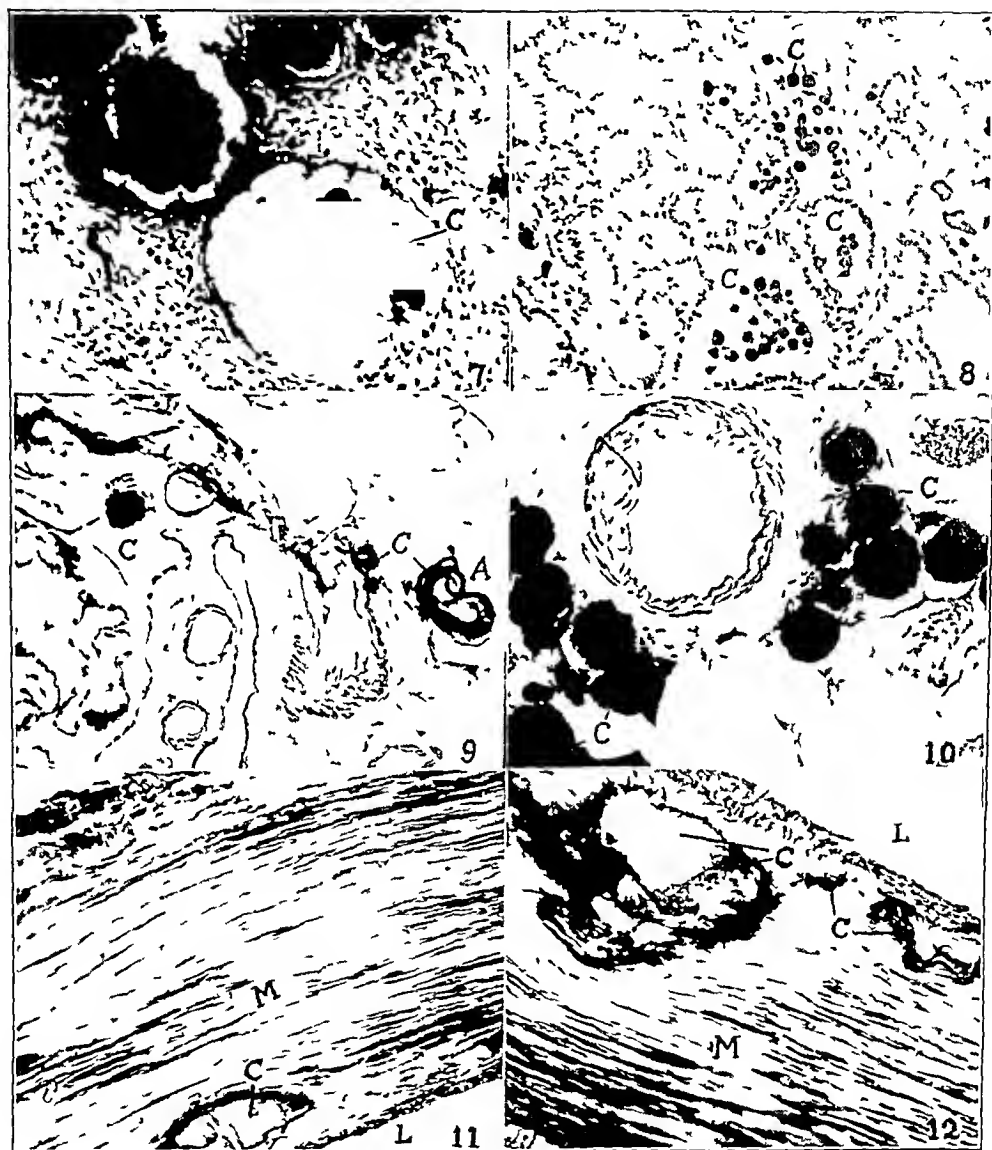
The deposits in this specimen showed areas of calcification commencing as a clumping of five or six small granules. The deposit, evidently caused by precipitation, was not intracellular nor in any special locations, but seemed to occur haphazardly. The larger masses produced by the aggregation of granules here showed imperfect fusion, as the small granules seemed to retain their individuality instead of the whole mass becoming one large crystal. The areas looked as though they would crumble easily into their original granular constituents if crushed.

A second specimen (fig 9) from the roof of the third ventricle had the appearance of having all its calcified areas contained in blood vessels. Cross-sections showed circular areas with the deposit in concentric rings, the whole area being surrounded by a dense fibrous wall. Sometimes such an area is seen in longitudinal section as a long calcified column in a fibrous wall. Occasionally the fibrous wall is also included as a densely calcified part of the deposit. Two or three such areas showed fractures on cutting, and here the calcified wall had split into layers (fig 9) in such a way as to suggest strongly its original character as the wall of an artery. The evident assumption was that calcification followed thrombosis in the plexus. The fine granular nature of the deposit was sometimes evident, but fusion into the large masses was much phosphate and a fair amount of iron combined with the calcium.

Microchemical methods showed the presence of little carbonate, much phosphate, and a fair amount of iron combined with the calcium. The carbonate was much less in amount than that found in the pineal gland.

Thyroid Gland—In the thyroid gland which was examined calcification was diffuse and widespread. In sections stained with hematoxylin, dark blue bodies, often several times the size of a cell, were seen in

PLATE 2



EXPLANATION OF PLATE 2

Photomicrographs of specimens stained with hematoxylin and eosin. Photography with use of Wratten color filters, done by Mr W C M Scott

Fig 7—Section of pineal gland showing large calcified masses, *C*, intensely stained, irregular contour of masses gives evidence of their formation by fusion of smaller spherules, $\times 60$

Fig 8—Section of thyroid gland showing densely stained spherules of calcium, *C*, lying in the colloid of the gland, $\times 60$

Fig 9—Section of choroid plexus from roof of third ventricle showing calcified masses, *C*, apparently in blood vessels, and at *A*, the calcified wall of an artery, fractured in cutting the section, $\times 60$

Fig 10—Section of choroid plexus from descending horn of lateral ventricle showing calcified masses, *C*, some with edges showing granular nature, $\times 60$

Fig 11—Section of arterial wall showing small crystalline calcium deposit, with only the periphery stained, and the center clear, at inner edge of muscular layer *L*, indicates arterial lumen, *M*, muscular layer, *C*, calcium deposits in this figure and in figure 12, $\times 60$

Fig 12—Section of arterial wall with larger calcified area with central clear area and stained peripheral region also two small areas of calcification densely stained $\times 60$

aggregations inside the colloid in the follicles. Examination of the unstained sections with the dark field and also with the polarizer showed that these bodies were clear, glassy, doubly refracting crystals (fig 8).

Many of these small crystalline deposits were round, but others appeared as triangular and quadrilateral plates, such as those which occur in experimental precipitation of calcium carbonate in colloids. Occurring as these bodies did, embedded in the colloid of the thyroid gland, the interpretation of their presence is that they were formed by precipitation, and their shape indicated that as in the case of the pineal gland their constitution might be almost entirely calcium carbonate.

Arteries.—Various arteries such as the radial, ulnar, anterior tibial and femoral were sectioned through calcified areas which were not too thick and heavy. In spite of this, some sections broke into many fragments while all were broken in some place or other. These fractures were often of benefit, however, by showing the way in which cleavage occurred in the calcareous masses, and much information could be gleaned from them.

The calcified areas were situated either just under the intima or else in the muscle layers, and varied in size from large masses a third of the circumference of the vessel down to minute spots whose diameters were only a few microns.

The calcified material showed the same features as noted in the case of the pineal gland and the choroid plexuses. Dark-field illumination of unstained specimens brought to view brightly lighted, clear, glassy, crystalline masses, doubly refracting when tested with polarized light. Stained sections showed intense affinity of the calcified area for hematoxylin (figs 4, 5, 6, 11 and 12).

Some areas appeared to contain the calcium salts in densely packed masses of granules which were shown in clouds at fracture lines where the edge of the mass had crumpled. Other areas were more definitely crystalline and where fractured, plates were split off in the form of triangular and quadrilateral crystals. These areas appeared to be the smoothest, and were usually large and therefore presumably older than other deposits. Some calcified regions appeared under the microscope as dense masses of material laid down in layers which seemed lumpy and uneven, and looked as though they had been formed by the close packing and fusion of rough spherical bodies. Such an appearance I have seen previously in calcium salts precipitated in albuminous solutions.

A peculiar fact noted in connection with the arteries was that in areas showing large calcified masses (figs 11 and 12) only the periphery of the mass was densely stained with hematoxylin. The remainder of the deposit, centrally placed and therefore older, was either only lightly tinged in color or else was entirely unstained. The unstained portion

looked in every way like a pure crystal, and was evidently in a form which had small affinity for hematoxylin. The newly deposited, more granular peripheral layer of the mass was of recent deposition, and its intense affinity for the stain recalled the madder experiments on bone, in which madder does not stain old bone, but does stain newly formed bone intensely. In the latter instance, Macklin has shown that this staining is due to the calcium which is being laid down in the bone at the time, forming a calcium lake with the madder dye. This intense staining is in line with the reaction which is seen in calcifying cartilage, in which the calcified portion is most intensely colored by the hematoxylin, and here of course the calcium is recently deposited.

In the crystals in the arteries, as time goes on there must be some reorganization in the crystal structure which changes its affinity for stains, recent deposits taking on the colors with avidity, old deposits being inert to them. This is in conformity with examples of reorganization in the crystals which I have described in a previous paper on experimental precipitation of calcium salts in colloids.

COMMENT

There are three aspects of the problem of calcification to be considered, namely, in what form calcium is transported to the tissues where it is deposited, under what conditions it is laid down, and by what means it is thus laid down.

Concerning the form in which calcium is carried in the blood there is no uniformity of opinion, but three fairly closely allied views may be considered as showing the possible ways in which this salt is transported. Pauli and Samec showed that in a colloidal albuminous solution, calcium carbonate and calcium phosphate are many times more soluble than in water. It follows that a reasonable amount of these salts could be carried thus in the blood practically in the form in which they will precipitate.

Holt, La Mer and Chown have demonstrated that blood serum is normally saturated up to 200 per cent with neutral calcium phosphate, and that this salt will remain for days without precipitating. They do not believe that most of the calcium is transported thus however but think it is carried as much more readily soluble acid carbonate and acid phosphates which may be converted into the neutral salts by loss of carbon dioxide.

From the latter view to that of Barillé is but a short step. He believes that calcium is found in the blood as a double salt, calcium carbonophosphate unstable and soluble only in the normal blood concentration of carbon dioxide. If the carbon dioxide content is anywhere reduced this unstable calcium carbonophosphate dissociates into its two constituents, which further are converted into the neutral carbonate

and neutral phosphate in the proportion in which these salts are found in bone

Wells has found this proportion of the two salts in bone fairly constant, approximately 15 parts by weight of calcium carbonate to 85 parts of calcium phosphate, or in the proportion of one molecule of carbonate to three of phosphate. He also states that in numerous areas of pathologic calcification the calcium salts are the same as in bone and in the same proportion.

The truth of any of these views cannot yet be accepted as definitely demonstrated, and yet the problem is most important as affecting our views as to the manner of deposition of calcium salts in the tissues, both in the normal process of bone formation and in the pathologic processes of calcification in various tissues.

It will be noted that there are several significant relationships shown in the pathologic deposits of calcium described in this paper. First, it is to be noted that the deposit is not associated with any one type of cell but occurs in many different tissues, second, there are no living cells included anywhere in the masses, such as are seen in the case of bone, third, there is no definite cellular membrane surrounding the mass to which its origin could in any way be ascribed, fourth, the masses of calcium are not even encapsulated or sheathed by fibrous tissue as though there was any tissue reaction to them.

The inference from the conditions just cited is that cellular activity is to be ruled out as the active agent producing the deposition of calcium in these cases. The only process of deposition left, therefore, is that of precipitation. If it is a process of precipitation, it ought to show the characters of the precipitation of calcium carbonate and phosphate in colloidal solutions, as shown originally by Rainey, and later by Harting, Biedermann, Watt and others. This is exactly what is shown, for the various forms peculiar to this process, such as spherules of various kinds, masses formed of irregular crystals, clumps of granules and a marked tendency of bodies thus formed to fuse, are found in the tissues studied. These forms are all characteristic of precipitation of calcium carbonate and phosphate in colloidal solutions, and lead inevitably to the conclusion that they were caused by the process of precipitation.

Views also vary as to the manner in which precipitation occurs in calcareous areas. A special affinity for special tissues, notably certain connective tissues, has been suggested, but in the present state of knowledge the suggestion has little meaning. Soluble salts reacting with carbonate and phosphate radicles in these locations does not explain why calcification occurs here and not elsewhere, and the supply of phosphate in such locations often seems insufficient.

The most logical explanation for precipitation is that put forward by Barillé, Wells and others that those calcium salts contained in solu-

tion in the blood and tissues are soluble only because of a fixed content of carbon dioxide in the solutions. If the amount of carbon dioxide is decreased, the salts precipitate. It can readily be conceived that in places of low grade activity, like necrotic areas, regions of fibrosis, thrombosed vessels and the colloid in the thyroid gland, there is probably little carbon dioxide, any fluids infiltrating these areas will have their concentration of carbon dioxide reduced, and their calcium salts will precipitate.

For certain areas of necrosis, particularly those in the walls of arteries, Klotz has advanced the idea that soluble sodium and potassium salts in the blood and tissues react with the fatty acids of the necrotic areas to form soaps, and by the reaction of soluble calcium salts with the soaps, insoluble calcium soaps are precipitated. In process of time, by the constant exposure of the soaps to the influence of carbonate and phosphate in the body fluids, a gradual conversion of the calcium soaps into carbonate and phosphate of calcium is accomplished. Klotz has demonstrated the presence of the fatty acids in the necrotic areas, and his ideas are given support by the conditions I have found in arterial walls, where the small, newer deposits, and also a few larger ones are granular, as one might expect the calcium soap to be. Older deposits are definitely crystalline and hard, this change of state agreeing with Klotz' idea of the gradual conversion of the calcium salts formed with the fatty acids into compounds of carbonate and phosphate. This change also explains the difference in staining between the center and the periphery of the large calcified masses in the arteries, where an intense blue is taken by the newly deposited peripheral layer with hematoxylin but the center remains clear and unstained.

SUMMARY

Areas of pathologic calcification were studied on human material from the pineal gland, the choroid plexuses of the lateral ventricle and third ventricle, the thyroid gland and various arteries.

The deposits were shown to be calcium by their optical appearance in unstained sections and their reaction to polarized light, also by staining reactions, by their removal by acids and by the similarity of their appearance to that of calcium salts precipitated in colloids.

There is no evidence of any cellular activity concerned in the deposition of the calcium salts. There is evidence for their appearance here by precipitation.

The precipitation may be originally in the form of carbonate and phosphate of calcium, or may be as a calcium soap formed by reaction with a fatty acid and later gradually converted into the carbonate and phosphate.

Iron was found combined with the calcium deposits in the nervous system.

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CHRONIC SEMINAL VESICULITIS AND PROSTATITIS

A FURTHER REPORT ON THE RESULTS OF OPERATIVE TREATMENT AND ITS INDICATIONS *

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In reporting a series of cases of about 200 patients operated on in association with Dr F W Smith in 1923, the symptomatology of seminal vesicle disease was classified into three groups with reference to symptoms. The first group included those cases in which pain is the predominating element with inflammatory changes, the second, those cases in which rheumatic symptoms are present, and the third those cases in which vague local symptoms are pronounced with an accompanying unexplained neurosis. Three years' further experience bears out the value of this grouping as a working scheme. Operative indications may be similarly epitomized, and these three clear and distinct reasons for surgical intervention and drainage may be given (1) the evacuation of pus, (2) the relief of pain and (3) the removal of hard, indurated fibrous vesicles productive of systemic, prostatic and bladder symptoms.

GROUP I PAIN AND INFLAMMATORY CHANGES

Infection of the vesicles occurs in practically 40 per cent of the cases of chronic gonorrheal urethritis when the latter becomes posterior. Ballenger and Elder stress the importance of ascertaining whether gonococci are actually present by the examination of a specimen of the semen. It is claimed that a few scattered pus cells are found in the semen when the prostate alone is involved, but a definitely larger number of polymorphonuclear cells are present when there is extensive infection of the vesicles. In chronic seminal vesiculitis, there is a lesser number of pus cells. It is not the inflammation within the vesicles themselves that is to be considered entirely, as the infection is definitely conceded to be a secondary one superimposed on a gonorrheal type. In a series of many cases examined, gonococci have been found present in less than 2 per cent, and then in lesser proportion to some other organism. As in infections elsewhere throughout the body with specific organisms, such as tuberculosis of the lungs, and other conditions, secondary invasion of organisms persists and accounts for the chronicity of symptoms. It accounts also for the acute attacks that occur subsequently, and in almost every case, for the production of pus. Staphylo-

* From the James B Brady Foundation of Urology

cocci of various forms—*Bacillus coli*, *Bacillus proteus*, *micrococcus catarrhalis* and various streptococci may be present. In one case, *Streptococcus viridans* was isolated. Evidently there is not any particular selective affinity on the part of the gonococcus for the cavities of the vesicles. Amebas have been reported to have been found recently in the vesicles. However, the gonococcus invades the region of the ampulla and the periampulla and the vasa deferentia with the same freedom that it invades the prostate, the prostatic capsule and the fascia. This is of great importance in the solution of conditions referable to the vesicles, therefore, in that purely perivesicular changes occur, varying from small cicatrized areas to large plaques of dense scar tissue. These are continuous with the capsule of the prostate, and constrict the vesicles, rendering them both incapable of emptying themselves and less resistant to infection. The presence of *Bacillus coli* in many of the patients who were examined, is probably due to the fact that this organism, and others as well, travel from the rectum and traverse the intervening tissues. When a habitat in the vesicles is found with adequate culture mediums, a focus is soon established.

Gonorrheal infiltration usually follows the ejaculatory ducts through to the floor of the urethra, and there is practically a complete elimination of the lumen of the ducts. In delivering vesicles in this type of case, the constriction will resist the extreme degree of manipulation necessary to mobilize them, and the organs can be dislodged from their normal position and brought into the wound without their contents being emptied. It is obvious, therefore, that rectal massage is useless, and many patients are worse after massage because the infection within the vesicle is stirred up by manipulation. There are varying degrees of these periprostatic and perivesicular changes. In some patients the several layers covering the prostate are fused and the whole lifts up like a firm leathery cover, in others, the infiltration is scattered and it is impossible to dissect away the individual layers. This infiltration may progress until it extends well up in to the postprostatic space and becomes fibrous in type. There is then a combination of pressure and inflammatory atrophy of the vesicles, and they exist only as two fibrous cords of almost tendinous consistency. Another type may be noted in which from intermittent or incomplete obstruction within the ducts or periampulla region, the vesicles become engorged and distended, with pressure atrophy of the muscle fibers. This process is comparable to that which takes place in distention of the kidney pelvis and the development of hydronephrosis and may continue until the vesicle is almost cystic. In the case illustrated herewith, it may be noted that the dilatation is extreme.

Deep perineal pain, tenderness over the ischiorectal space and extensions of inflammatory processes which in general have had their

inception in a prostatic abscess, present immediate reasons for drainage. Frequently these infections will first extend down into the epididymis, involve the Cowper's glands, extend back to the prostate again and then break through the prostatic capsule. If this type of case is recognized at the outset, a prolonged convalescence can be prevented by perineal section and multiple incisions into the prostate. This is usually sufficient. If the process continues, it is most likely to extend upward and rupture into the superior pelvirectal space. This rupture is accompanied by a definite relief of symptoms comparable to the rupture of the appendix in an acute appendicitis, however, the relief is of longer duration. The temperature then subsides, and the loose areolar tissue of the space fills slowly with pus and drains the infected area about the prostate and vesicles. The rectum is gradually lifted upward and backward and fully a quart of pus collects before localizing symptoms again appear. Heretofore, the infection in the prostate has been under pressure, with obvious pain and temperature reaction. Symptoms again appear in the nature of rectal difficulties. The patient complains of constipation and difficulty in evacuating the stool, although constipation may never have existed before. The surgeon, being accustomed to examining the prostate, feels this, and if unmindful of developments may possibly miss the pathologic condition farther up in the rectum. If the rupture has occurred around the margin of the base of the prostate where Dénouvillier's fascia dips back to enclose the vesicles, the bulging rectal mucosa may be noted. Generally, however, a proctoscopy will confirm the diagnosis.

CASE 1—G W B, aged 36, married, was admitted to the United Hospital, Portchester, complaining of pain in the suprapubic region. He had slightly increased difficulty in urination and his temperature was 102 F. There was a past history of gonorrheal infection. The patient had married since being infected, and had two children.

Rectal examination showed the prostate swollen and tender. The urine was cloudy and contained pus cells and sediment. The patient was treated with rectal irrigations and routine medical measures for four days, after which time the swelling of the prostate subsided slightly. Two attacks of acute retention occurred, for which the patient had to be catheterized. This was accomplished without difficulty. The temperature continued at 100 F for several days and then began to show a septic curve, rising to 102 and 103 F daily. There was less urinary difficulty, and the prostate was not particularly tender, nor did it increase in size. There were considerable loss of weight and general malaise, the blood count was 15,800.

Two weeks after admission the patient began to complain of pain in the sacro-iliac region and some sensation in the right leg. This gradually increased, and on rectal examination there was a moderate fullness posterior to the prostate. Rectal irrigations were again instituted, but the swelling increased, extending down to the sulcus to the right of the prostate. A slight tenderness could be made out over the right ischio-rectal space.

Diagnosis of prostatic abscess was made, and it was decided to operate. A perineal incision was made, and the prostate was exposed in the usual manner. The posterior capsule was stripped away and the dissection carried up posterior to the seminal vesicles, where a large abscess containing fully 10 ounces of pus was evacuated. From this point, the finger could be carried laterally to the abscess cavity as it was carried forward into the right ischio-rectal space, the areola had been entirely destroyed. The superpelvo-rectal cavity was drained directly, and a counter drainage was established through the ischio-rectal space. The patient made an uneventful recovery, and has been well since that time. When recently heard from his condition was good.

GROUP II RHEUMATIC SYMPTOMS

Rheumatism is the principal symptom associated with chronic vesiculitis. In this connection the following characteristic of posterior infections may be noted. If there is a complication with an original urethral infection, the same complication is likely to occur with subsequent attacks. For example, if from five to ten days after the onset of a urethral infection epididymitis develops, the same complication will occur in subsequent infections. This is also true when joint symptoms occur. If there is a recurrence, as is likely in 90 per cent of the cases, or if there is another attack, it will be accompanied by a return of the rheumatic symptoms. This early development of complications signifies one of two important clinical facts: the infection is a severe one, or resistance is not great. In almost 95 per cent of the cases of gonorrheal rheumatism, the latter is true. As rheumatism is seldom seen as a complication in private cases, but rather in hospital cases, usually in the municipal hospitals, the problem takes on an economic aspect. What is the best method of reducing the hospitalization time of these patients, provided that it does not detract from the efficacy of treatment for the original condition?

The answer to this is prostatotomy and seminal vesiculotomy. This not only cuts down the time of the first attack, but lessens the incidence of an associated rheumatism with subsequent attacks. The focus of infection within the prostate or vesicles, if isolated by circular inflammatory changes and scar tissue as described above, acts as definitely as diseased roots or apical abscesses in causing rheumatic joint symptoms.

GROUP III LOCAL SYMPTOMS AND NEUROSIS

The third group of cases may be attributed to inflammatory changes that have extended backward and involved the trigone and neck of the bladder. The infection extends to just beneath the mucosa, with involvement of the muscles of the trigone. This may give rise to various disorders of urination, such as a sense of incomplete emptying, difficulty in starting the stream and tenesmus. There may even be perineal pain and a sense of fulness in the perineum and at the neck of the bladder. The patient may say that the neck of the bladder feels stiff after urinat-

ing, as if the bladder wall could not fully contract. This is due to stiffened, unyielding vesicles which extend out onto the bladder wall like a pair of brackets converging to the vesical neck and adherent to the bladder wall. One author reports a case in which extravasation occurred at the site of the vesicles and extended forward along the usual fascial plane, and it was only in radical incision of the perineum that he noted the opening in the bladder at this point. He cites the possibility of this factor being present in other cases of extravasation, and states that abscess formation in the vesicles with destruction of tissue together with a firm stricture anteriorly may account for the extravasation. The cystoscopic examination reveals a well defined trigonitis in many cases, and occasionally the outline of the distended vesicle can be seen showing through the bladder floor. Injected vessels in an area limited by the outline of the vesicles have occasionally been noted. The results of the cystoscopic examination are confirmatory, however, rather than absolutely diagnostic, and serve to explain the bladder symptoms frequently found and mentioned by numerous investigators.

The factor of chronic vesicle inflammation in impotence is a difficult one to judge. It would seem that infection of the vesicles exists in at least 65 per cent of the cases of impotence; however, it does not follow that this could be cured by operation. This eliminates a large number of so-called neurotic cases, in which the so-called "sexual neurosis" of the patients is attributable to chronic vesicle infection. Interference with the nerve supply as a result of the perivesiculitis, together with a lessened capacity of the vesicles, accounts for the impotence and associated symptoms of which these patients complain. It is true, however, that cures or even relief can be expected to a lesser degree in this class of cases than in any other, and operation may make their condition worse.

It might be noted that as a factor in persistent discharge vesiculitis plays an insignificant rôle and reference to the tables will readily demonstrate this. Twenty-two cases were seen with a view to operation for persistent discharge, leukocytes were found, the duration of the condition was more than a year. Seven cases were considered suitable for operation. Five patients showed a marked degree of improvement sufficient to justify the procedure, two were slightly improved. An operation should never be considered in these cases until massage has been tried. It may be that the retention within the vesicle is due to the pressure of a distended and boggy prostate on the ducts. If, however, extensive inflammatory and suppurative processes have existed, it is probable that the ducts are stenosed and the symptoms thereby aggravated. However, massage often gives satisfactory results. The following case is illustrative.

CASE 2—C C, admitted to St Bartholomew's Hospital Clinic, had been treated three years before for gonorrheal infection which was accompanied by a severe prostatitis and posterior urethritis. Irrigation and the usual measures of treatment were used, under which discharge subsided. One year after the original infection, the patient developed a pain in both knees, which made it necessary for him to discontinue work. At times he walked with the aid of a cane. Further examination showed the prostate markedly distended and hard, this disappeared on vigorous massage, followed by rectal irrigations. The patient said that there was immediate relief of symptoms following massage. Gonococci were demonstrable in material obtained from prostate. Following the lessened presence of pus cells in the secretion, the ejaculatory ducts were catheterized and irrigated with 1 per cent solution of mild silver protein. A marked

TABLE 1—Symptoms and Treatment in Series of Cases Discussed

Cases		Average Duration	Treatment	
			Operative	Palliative
19	Acute arthritis	5 weeks	11	8
11	Chronic arthritis	6 9 months	11	
19	Urinary disturbances	5 months	7	12
27	Chronic discharge	1 year	7	20
9	Dysuria	6 months	2	7
11	Impotence	?		11
4	Right-sided and left-sided pain	6 months	2	2
6	Epididymitis	6 months	4	2
7	Pyuria	?	5	2
2	Acute retention		0	2

TABLE 2—Results of Operative and Palliative Treatment

Operative			Palliative		
Cured	Improved	Unimproved	Cured	Improved	Unimproved
9	2			2	6
9	2				
4	1			5	14
5	2		2	13	5
2				3	4
1	1			1	1
3	1			1	1
4	1		1	1	
				1	1

improvement was noted, and four months after the beginning of the treatment the joint symptoms had disappeared entirely. It was noted that the edema of the ejaculatory ducts which was present at first had entirely disappeared, and a bougie could be passed without pain. Roentgenograms of the joints did not show prominent joint changes. Three years after treatment the patient was still free from pain.

In some cases a bougie or fine sound passed into the ducts through a urethroscope is effective in reestablishing drainage. This measure should always be utilized and is most useful when patients complain of deep-seated pain after coitus, when the pain is due to stricture of the ejaculatory ducts, dilatation often brings about a relief of symptoms.

Seminal vesicle disease should be borne in mind likewise, in conditions of the upper genito-urinary tract when ureteral obstruction is

evident Ureteral stricture due to extrinsic causes—periureteritis, and other conditions, often results from infection elsewhere in the body. Infected teeth, root abscesses and diseased tonsils are ready sources of origin. Less remote is the extension of infection from the adjacent vesicles. The relationship of these structures is marked. The process is periureteral, and infiltration of the ureteral wall is not present. In cystoscopic examination in these cases, the orifice on the affected side will be noted as occupying an abnormal position. It is usually pulled externally as the contraction seems to extend in that direction rather than toward the midline of the bladder. Cystoscopy likewise often gives a direct clue to the nature of the infection. In the injected and congested trigone, the outline of the vesicle can be noted through the mucosa, and in well defined cases the vascular outlines follow more or less accurately the shape of the vesicle. Cystoscopy should not be overlooked, therefore, in attempting to arrive at a diagnosis, and any abnormality in the position of the ureter should be noted. In strictures and narrowings just above the orifice, the vesicle should be examined.

In tuberculosis of the lower tract, the disease is likely to extend to the ureter when once the prostate and vesicles have become involved. In this case the ureteral constriction is more marked. The cystoscopic changes are characteristic, but the infiltration of the ureter often makes it impossible to catheterize the ureter. The infection spread from the tissues and fasciae around the vesicle, anteriorly and involves the muscle of the bladder. Considerable resistance is offered at first, and there is a tendency for cicatrization and involvement of the trigone and orifice. It would seem that a tuberculous ulceration might occur, but this is never seen. The process involves the ureter, infiltrating first the muscular layer. Edema of the mucosa occurs, but slowly, apparently, as there is never a history of renal colic. Finally, a small channel remains in the ureter through which the kidney can excrete. It is impossible to introduce the finest bougie into the ureter. The mucosa is easily traumatized and bleeds, and after one attempt it is impossible to try again for three or four weeks. Tubercle bacilli are seldom found, and, if present, one cannot be certain that they have not come from the kidney into which there may have been further extension. Usually a firm scar forms with retraction of the orifice upward and backward. Its real position is easily recognized, and with one finger in the rectum, palpating the vesicle, and the cystoscope in position, the orifice can be seen to move as if it were a part of the vesicle itself. I have seen seven such cases.

CASE 3—A man, aged 32, married, complained of loss of weight, marked discomfort in the perineum and at the neck of the bladder, together with nocturnal frequency. Two months before he consulted me, he had noted marked increase in nocturnal emissions, at one time he averaged one a night.

The left epididymis was slightly increased in consistency, but nodules were not made out. The left seminal vesicle could be palpated as a definitely indurated prominent stricture in the postprostatic space, it was moderately tender. A preliminary diagnosis of tuberculosis of the seminal vesicle was made, and the patient was advised to have cystoscopy performed. This was done the following day. A marked trigonitis was found with injection in the region of the left vesicle, the left orifice was pulled upward and outward, and an attempt to pass a ureteral catheter was followed by rather free oozing. Several types of catheters were tried without success. The patient did not have a reaction for three days, when a marked left epididymitis developed. He went into the hospital for one day, and the pain and swelling subsided. A specimen of the urine which was injected into a guinea-pig was reported negative. Three months after examination the patient was seen again. Two small nodules were present in the left epididymis, and the vesicle was still tender and swollen. The patient's bladder had been irrigated twice a week during the interval. It is probably that this reduced the changes near the ureteral orifice, but the patient would not allow this to be confirmed by cystoscopy.

Diagnosis of tuberculosis of the right vesicle, quiescent in type, seemed unquestionable, and was confirmed by a consultant who also saw the patient.

CASE 4—D F D, aged 23, unmarried, complained of frequency of urination and a sense of fullness in the perineum and occasional swelling of the left testicle and the epididymis. Both vesicles were palpable, the left more so than the right, and distinctly swollen and tender. The patient complained also of pain in the region of the left kidney, and the organ was slightly enlarged and lower than the opposite kidney. Cystoscopy showed an injected trigone and neck of the bladder, the ureteral orifice was elevated and pulled upward and inward. It was impossible to catheterize it, although attempts were made on more than ten different occasions. An injection of indigo-carmin showed a return two minutes later in the opposite side and a dye issue in a fair sized swirl.

Diagnosis was made of left tubercle seminal vesiculitis, localized, with tuberculous stricture of the ureter. The patient was observed for two years, but has since disappeared from observation.

Young has reported good results in the treatment of tuberculosis of the lower tract, epididymis, vas and vesicles by removal of the organs en masse. His results are unusual, however, and generally much improvement cannot be expected. This process is as likely to be cured under hygienic treatment as by operation. Difficulties are encountered at every stage, the possibility of spreading the infection within the inguinal canal is not remote, urethral fistulas are not uncommon, and the perineal wound heals with difficulty. When palliative measures, as recommended, have been given a fair trial, a perineal operation with the exposure of the vesicles and removal or thorough drainage is indicated.

OPERATIVE PROCEDURE

The patient should be in the so-called exaggerated lithotomy position, described by Young, as the operative procedure is much facilitated. The sacrum is elevated from the plane of the table and the buttocks brought out over the edge, which brings the perineum almost parallel

with the floor—a great advantage in all perineal procedures. A curved incision is then made starting from the ischial tuberosities and continuing through a point which is just superficial to the termination of the bulbous urethra. This point can be determined by palpation of the perineum on a sound which has previously been placed in the urethra. The central portion of the incision should be carried to a depth of at least 0.5 cm. This measure is important, as it provides for better healing

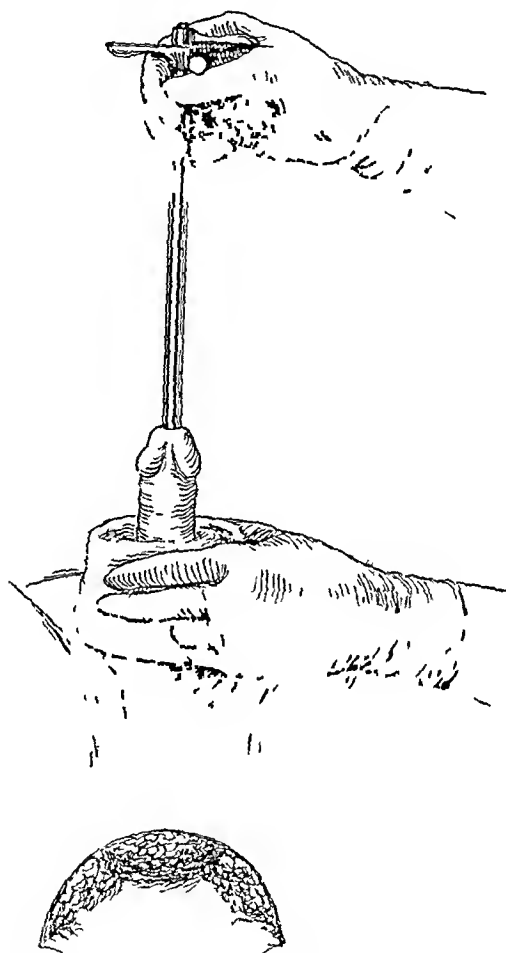


Fig 1—Seminal vesicle tractor in position and line of incision. This incision is carried much deeper in the center than at the sides, and the upper angle of the wound corresponds to the junction of the bulb and membranous urethra. If this precaution is observed, there is much lessened possibility of hemorrhage.

of the central portion of the skin flap. In a large series of cases we failed to obtain a sloughing of the triangular portion at the end, as is often seen when an inverted V incision is made. Retraction of the skin flap exposes the site of the central perineal tendon, the tendon is divided sharply after blunt dissection of the lateral fossae on either side. At this point it is important to proceed carefully and retain all the fibers of the bulb in the upper portion of the wound. The thin

fibrous line of the central tendon, as it converges toward the bulbo-membranous junction, can be plainly seen. This prevents a great deal of bleeding from the vascular bulb.

The sounds should then be removed from the bladder and a seminal vesicle tractor inserted (fig 1). Traction on this pushes the prostate forward and elevates the apex. By careful sponge dissection after previous introduction of the finger into the rectum, it is possible to strip away from the apex of the prostate the well defined attachments of the recto-urethral muscle. At this point the muscle becomes prominent, and it is necessary to guard against injury to the rectum. In observations on numerous operations in which the rectum has been injured, precautions regarding the rectum are usually taken prior to this time, since here the rectum and prostate are in close relation.

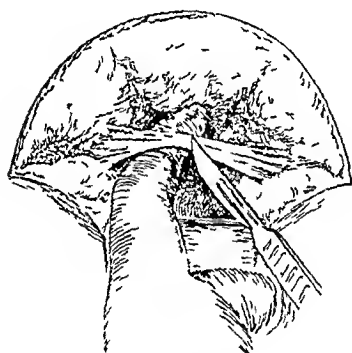


Figure 2



Figure 3

Fig 2—Division of the superficial transverse muscle of the perineum with exposure of the recto-urethralis and the deeper structures.

Fig 3—Elevation of the muscular layer of the recto-urethralis from the urethra and apex of the prostate.

Gentle tension on the flap with one finger in the rectum stretches these fibers, and they can be divided with the scissors close to their insertion in the urethra (fig 2). When the rectum has been separated from over half of the anterior surface of the prostate, the remainder of the procedure can usually be accomplished by gauze dissection. The free edges of the levator ani at this point come into view and they can be lifted gently from the posterior surface of the prostate and separation continued by hooking the finger under the free edge of the muscle and further detaching it, after which it can be retracted from the wound (fig 3).

The posterior surface of the prostate now comes into view, and this should be cleansed of a few adherent fibers (fig 4) of muscle tissue and other debris which have remained from the removal of the rectal wall. This is best accomplished by the handle of a knife, and the white capsule

of the prostate is distinguished by its fascia-like character. The prostate is then retracted firmly into the wound and an incision made transversely, at a point just behind the middle axis of the gland. Numerous engorged blood vessels, the latter the result of the vesicular infection, frequently can be noted in the tissues, and the incision can be varied to avoid these. If sectioned, they give rise to troublesome bleeding. At this point care should be taken to recognize the existence of a special fascial plane

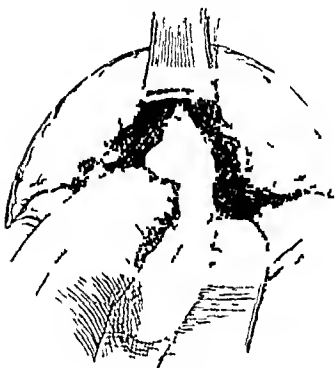


Figure 4

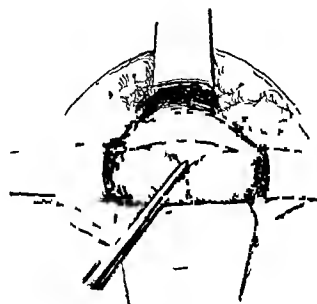


Figure 5

Fig 4—Stripping off the fibers of the recto-urethralis with gauze sponge and beginning exposure of the apex of the prostate

Fig 5—Elevation of the prostate into the wound by means of the tractor and division of the two layers of the prostate fascia which covers the prostate posteriorly and involves the seminal vesicles

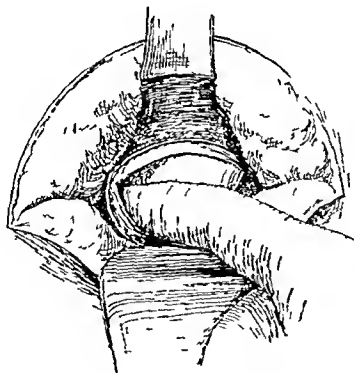


Fig 6—After a line of cleavage is obtained, Denonvillier's fascia can be stripped from the prostate by the index finger

covering the vesicles, and after division of the first layer of the fascia, a second layer should be identified and stripped back in order to reach the vesicles (fig 5). The tip of the index finger is then inserted anterior to the fascia and along the posterior surface of the prostate, extending outward, and the vesicles can be palpated (fig 6). Pressure on the organ will sometimes expel a moderate quantity of vesical contents through the urethra. Enucleation is then begun at the tips of the

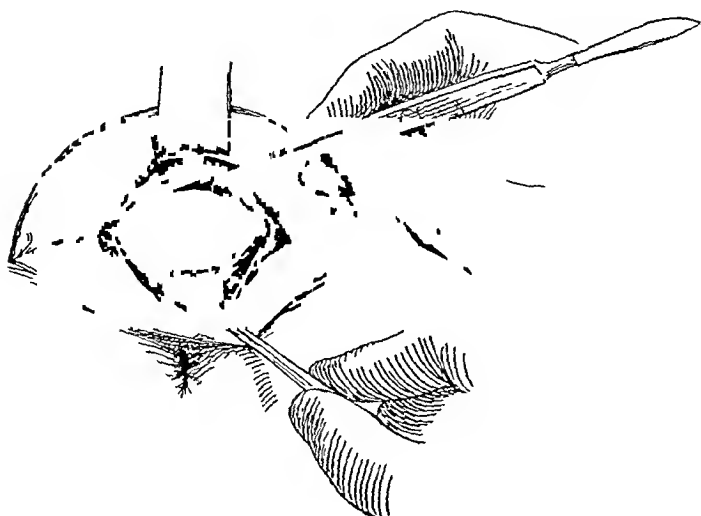


Fig 7—Removal of one layer of Denonvillier's fascia and separation of the second layer. If these layers are removed separately, there is less danger of the finger rupturing posteriorly into the rectum.

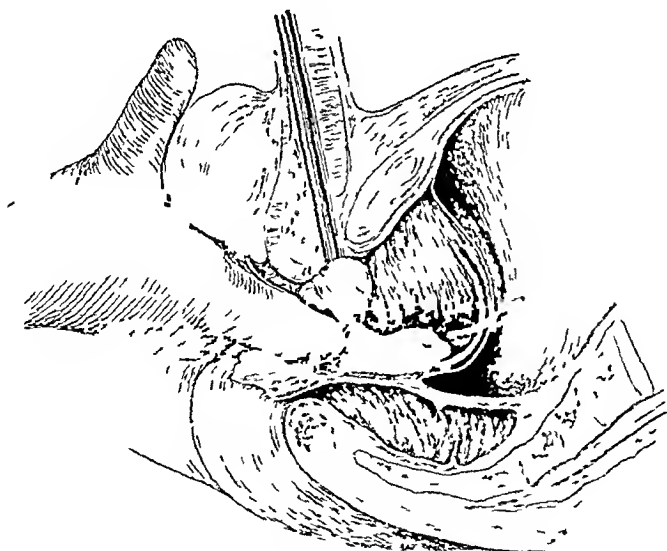


Fig 8—Sagittal section, showing the extravescicle and extraprostatic limitations of the enucleation. The finger is carried posterior to the prostate and in front of the two layers of the prostatic capsule to the tip of the vesicle, which, as may be noted, lies just before the point at which the ureter enters the bladder. There is scarcely any danger of injury to the ureter. Enucleation is carried out by dislodging the tip and finding a line of cleavage between the vesicle and the floor of the bladder. In cases of prolonged inflammation this may be difficult.

vesicles until they are freed. Numerous adhesions to the base of the bladder are noted, but these can be broken through without difficulty, further adhesions between the vas, which at this point is directed internally toward the ampulla, are likewise separated (fig 7). A gauze sponge on a holder, if introduced into the postprostatic space, is often of assistance in drawing the entire structure forward, and the rest of the procedure can be completed under the guidance of the eye (fig 8).

In vesiculotomy, an incision is made in the vesicle at the point where it joins the ampulla, and numerous incisions are made along the axis of the organ. The vesicle is crushed at this point and then excised (fig 9). The necessity of ligation has not been noted, although

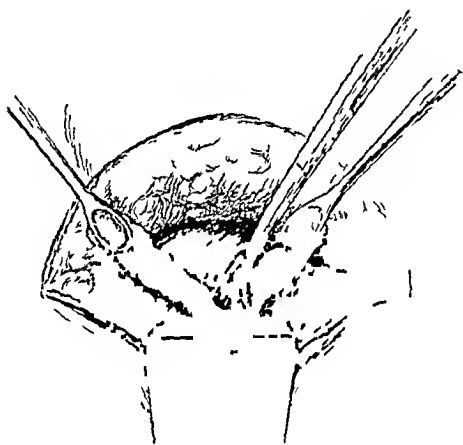


Figure 9

Fig 9—Delivery of the seminal vesicle into the wound with clamp in position for left vesiculectomy.

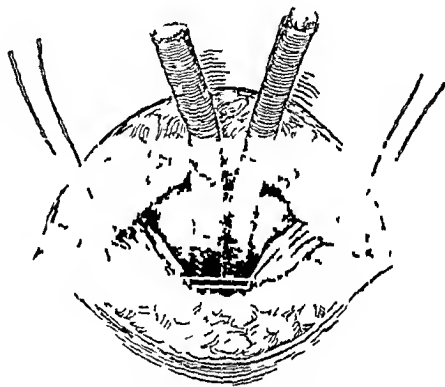


Figure 10

Fig 10—Closure of the wound. The drains extend posterior to the prostate, the vesicles after section or removal have been replaced. A heavy suture through the two levator ani muscles serves to obliterate almost the entire cavity. A second suture can be placed superficially.

ligation may be done. It is wise to determine the presence of this secondary layer of fascia. In some operative procedures, the prostate is excised too deeply, and when the finger is inserted posterior to the prostate, the vesicles cannot be felt because, together with their fascial coverings, they have been forced down beneath the level of the finger.

The prostate is incised liberally, drainage tubes or wicks inserted at the site of excision or incision and the prostatic capsule sutured in two places. The sound is withdrawn from the urethra and a loose suture placed in the edges of the levator ani muscle, this is drawn over the prostate and the central tendon is remitted (fig 10). Further sutures are not taken, except in the skin, which is closed with interrupted silkworm gut, the tube is brought out on each side of the central portion of the wound.

There is often excessive bleeding, as seen in all other operative procedures on the bulb and the perineum, such as strictures of the urethra, external urethrotomy, etc. The oozing following the separation of the vesicles from the base of the bladder may be considerable. Packing is sufficient to check this, but occasionally the oozing continues, and when the subsequent clot breaks down, convalescence is measurably hastened. If two rubber tubes or pieces of catheter, size 28 to 30 French, are introduced with the packing, the clots may be washed out and irrigation carried on through them for two to three days at most (fig 11). The tubes may then be removed.

Convalescence is generally uneventful. Before using the tubes in addition to packing, several hemorrhages are likely to occur, and convalescence may be prolonged unduly. This difficulty has now been overcome. Rectal injuries may and do occur. The rectum may be

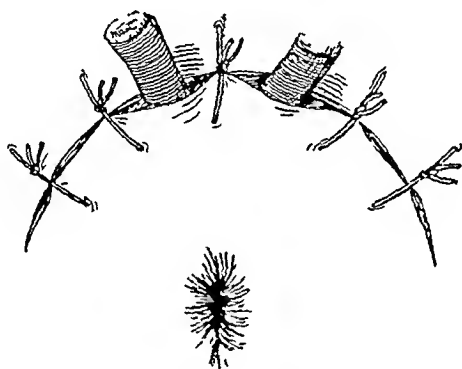


Fig 11—Closure of the wound with two cigaret drains extending into the seminal vesicle cavity. This technic is now modified by the inclusion of a catheter introduced together with the wicks for irrigation.

cut or the point of the retractor torn through the wall. All these lesions heal without incident, more than ten or twelve days are seldom added to the period of convalescence.

COMMENT

The specimens removed at operation showed a variety of pathologic changes. Early workers in this particular field determined that the process was almost entirely a perivesicular one, and scar tissue with mononuclear infiltration comprised most of the tissues removed. Dillon and Blaisdell have comprehensively grouped the changes into two classes—those involving the intrinsic structures and those involving the extrinsic processes. In numerous patients operated on, I have noted considerable scar tissue in the prostate. Microscopic sections have shown at times fibro-adenomatous hypertrophy of the prostate.

In these patients the vesicles are usually cystic and greatly dilated. There may be simple engorgement of the subepithelial blood vessels to round cell infiltration of the wall, with formation of granulation tissue and organized exudate which incorporates the tip of the vesicle to the extent that it cannot be freed. In patients in whom the vesicles have been the seat of an inflammatory process, the vesicles are atrophied and form two thickened branches of scar tissue which have lost all semblance of their original anatomic contour. A type similar to this is seen in tuberculosis, but with less atrophy. The tubercle bacillus invades the wall of the vesicle, and infiltration continues at the expense of the cavity, which is finally obliterated. The cavity is filled with an inspissated cellular debris which contains broken-down epithelium, red blood cells and occasionally, if there has been a recent inflammatory process, leukocytes and free pus. It is in this type of case that there will not be any reaction to treatment, and in which improvement must result from operative measures. The accompanying prostatic involvement is of great significance. Free incision of the capsule both laterally and beneath the ejaculatory ducts relieves the hyperemia, and prolonged drainage changes the cellular structure to a degree that the constriction of the ejaculatory ducts is relieved. When the vesicles are drained or removed, the ampulla undergoes a similar change if inflammatory changes persist in the prostate.

In the first group of patients in which pain is the predominating element, there is immediate relief, particularly when a quantity of pus is evacuated. When there is dull, throbbing prostatic pain, regardless of free pus, relief is obtained in the same manner. In cases in which rheumatism is present, pus is evacuated, and the most recent joint involvement disappears. If all joint symptoms have been acute, the pain and swelling quickly subside. If there is inflammation of the knee, greater freedom of motion is soon noted and lessened pain, but the swelling persists. These patients derive benefit from the application of intense heat, which promotes absorption of the exudate. In general, results are most satisfactory.

In the third group, in most cases the results are not as satisfactory. Operative indications cannot be said to be as definite, and surgical intervention is generally employed after a prolonged course of various other forms of treatment. While convalescing, these patients should be treated systematically with irrigations of the bladder and applications to the vesical neck and trigone. It is difficult to follow all of the patients in this way, and this lack of individual attention may explain some proportion of the failures.

CONCLUSION

Infection of the seminal vesicles and perivesicular tissue occurs as a complication of gonorrheal infection, and persists after the original infection has apparently subsided

Persistent and latent infections of the vesicles give rise to three definite groups of symptoms

Patients with cases belonging to these classifications should be operated on, and there should be surgical drainage of the vesicles, prostate and adjacent tissues

Operative procedure, beyond prescribing technical difficulties common to all perineal sections, is not serious, or attended with unusual danger to the patient

Results, from the standpoint of relief from symptoms, lessened physical disability and shortened convalescence, justify a continued and more frequent use of this method

HYPERTROPHIC ARTHRITIS OF THE SPINE

ITS INCIDENCE AND NATURE IN PATIENTS MORE
THAN FIFTY YEARS OLD *

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In the Section on Roentgenology at the Mayo Clinic the incidental occurrence of hypertrophic arthritis of the spine in middle-aged and elderly persons with other diseases has attracted more than passing interest, and led to this study to determine the incidence and nature of the disease among such patients. The study of incidence was based on the cases of 2,090 patients more than 50 years of age, who were referred to the section for roentgenograms of the kidneys, ureters and bladder during the year 1925. This particular group was selected because in the roentgenogram of the genito-urinary organs the spine is clearly shown incidentally. A suspicion of disease of the spine was not included in the reasons for reference except in a small percentage. Such cases are usually referred explicitly for a roentgenogram of the spine itself. This study of the nature of this disease is based on a detailed analysis of 500 cases showing hypertrophic arthritis of the spine. The chief complaints of the patients on admission, complaints possibly spinal in origin, evidences of senescence, the presence of apparent and possible foci of infection and the incidence of obesity have been considered. Note was also made of the final diagnosis in each case.

INCIDENCE

The incidence of hypertrophic arthritis of the spine, based on the total group of 2,090 cases is shown in table 1. The predominance of men is explained by the large number of cases of hypertrophy of the prostate in the group, as it is a routine procedure at the clinic to obtain a roentgenogram of the kidneys, ureters and bladder before cystoscopy.

DETAILED ANALYSIS

Of the 500 patients selected indiscriminately from the group with arthritis of the spine, 160 were women and 340 were men, and in the analysis the sexes are considered separately as regards presenting complaints, diagnosis, and other factors. The chief complaints of the women in this group are indicated in table 2, and those of the men in table 3.

* Thesis submitted to the Faculty of the Graduate School of the University of Minnesota in partial fulfillment of the requirements for the degree of Master of Science in Medicine, April, 1926

The disproportionate number of urinary complaints is due to the large number of cases of prostatic disease in patients more than 50 years of age. The many cases with abdominal complaints in such a group of roentgenograms are explained by the fact that often the presence of an obscure or indeterminate abdominal symptom not clearly related to any viscus will prompt the clinician to refer the patient for roentgenographic examination to determine whether the urinary tract is involved.

TABLE 1—*Incidence of Hypertrophic Arthritis of the Spine with Other Diseases*

	Total Cases	Arthritis	
		Cases	Per Cent
Men	1,415	939	67
Women	675	271	40

TABLE 2—*Chief Complaints of Women with Hypertrophic Arthritis of the Spine*

	Cases	Per Cent
Gastro intestinal and indefinite abdominal disease	57	55.6
Genito-urinary disease	42	26.2
"Rheumatic" and neuromuscular disease	23	16.3
Weakness, nervousness, anorexia, etc	16	10.0
Miscellaneous headache, dyspnea, heart trouble, goiter, rectal trouble, edema and diabetes, indefinite	19	11.9
Total	160	

TABLE 3—*Chief Complaints of Men with Hypertrophic Arthritis of the Spine*

	Cases	Per Cent
Genito urinary disease	205	60.3
Gastro-intestinal and indefinite abdominal disease	52	15.3
"Rheumatic" and neuromuscular disease	34	10.0
Nervousness weakness, fatigue, etc	17	5.0
Indefinite	17	5.0
Miscellaneous chills, heart trouble, dizzy spells, goiter, palsy, etc	15	4.4
Total	340	

TABLE 4—*Incidence of Complaints of Backache, Lumbago or Sciatica*

	Total Cases	Backache, Lumbago Sciatica	
		Cases	Per Cent
Men	340	89	26.0
Women	160	62	33.7

It will be noted that there were but sixty patients in both sexes with rheumatic, neuromuscular or definite disease of the joints as the chief or presenting complaints. However, the specific complaints of backache, lumbago and sciatica were given as chief or secondary symptoms in a somewhat larger number of cases some of which are of course included in the general classification as "rheumatic" and so forth (table 4).

It will be seen, therefore, that 74 per cent of the men and 61.5 per cent of the women with hypertrophic arthritis of the spine had no accompanying complaint of the various types of rheumatic and neuromuscular pains. That there should be many patients with definite spinal changes without symptoms is rather to be expected, and has been observed by other writers on the subject. Nissen¹ has noted that the condition may exist for years and give no symptoms until there has been a sprain, a strain, a chilling of the body, fatigue or some other exciting cause. The subjective symptoms, according to Goldthwait,² are usually slight in comparison to the actual pathologic change, so the condition is discovered incidentally. Rosenheck³ comments on the fact that one may see extensive disease of the vertebrae with practically no radicular involvement. Radicular involvement with hypertrophic arthritis of the spine has been noted as a cause of abdominal pain. However, there were no cases in this group of 500 in which pain in the abdomen could be attributed only to the spinal arthritis. Parker and Adson⁴ have reported only eight cases seen at the Mayo Clinic from August, 1922, to November, 1924, in which there was definite suffering from a compression of the spinal cord or its roots due to hypertrophic osteo-arthritis of the spine.

In tables 5 and 6 the primary diagnoses in the 500 cases with arthritis of the spine are given in the order of their frequency, those of various pathologic conditions in the genito-urinary tract naturally predominating among both men and women.

Seventy and six-tenths per cent of the diseases of the urinary tract among men are comprised of prostatic disturbances. In addition to the various primary diagnoses of prostatic disease given in table 6, the prostate was involved secondarily as benign hypertrophy in seventy-one, as prostatitis in seven, and as a postoperative condition in two other cases, a total of 253 out of 340 cases in which the prostate was affected.

CAUSES OF HYPERTROPHIC ARTHRITIS

The same three factors that are the cause of disease in general cause arthritis: (1) infection, (2) retrogressive or metabolic changes and (3) irritation, chronic or acute. These three causes may act alone or

1 Nissen, H. A. Some Observations on Arthritis, *M. Clin. N. Amer.* 8: 1789, 1925.

2 Goldthwait, J. E. Osteo-arthritis of the Spine. *Spondylitis Deformans*, Boston M. and S. J. 141: 128, 1899.

3 Rosenheck, C. Radicular Pain and Its Relation to Spondylitis Deformans from a Neurological Viewpoint, *M. J. and Rec.* 122: 215, 1924.

4 Parker, H. L., and Adson, A. W. Compression of the Spinal Cord and Its Roots by Hypertrophic Osteo-arthritis, Diagnosis and Treatment, *Surg. Gynec. Obst.* 41: 1, 1925.

in combination. The classification of arthritis used at the clinic, excluding specific and neuropathic forms, is (1) infectious (nonspecific), (2) senescent and (3) traumatic.

Infectious, nonspecific arthritis may produce roentgenologic changes of a purely periarticular type, hypertrophic or destructive changes in bone, or atrophic changes in bone and cartilage. This infectious nonspecific type is characterized by its situation in many large joints or in the proximal and middle joints of the fingers, and occurs primarily in adults between the ages of 20 and 40. Cold, clammy hands and hypotension are two prominent symptoms.

TABLE 5—*Primary Diagnosis in Cases of Women with Hypertrophic Arthritis of the Spine*

	Cases	Per Cent
Genito urinary diseases: carcinoma of bladder, cystitis, pyelonephritis, cystocele, hydronephrosis, renal stone, urethritis, carcinoma of kidney, urethral caruncle, fibrosis of the bladder, etc.	55	34.4
Cholecystitis, with and without stones	27	16.9
Arthritis	17	10.6
Miscellaneous: myocardial degeneration, chronic nervous exhaustion, migraine, constipation, duodenal ulcer, appendicitis, inguinal hernia, etc.	61	38.1
Total	160	

TABLE 6—*Primary Diagnosis in Cases of Men with Hypertrophic Arthritis of the Spine*

	Cases	Per Cent
Genito urinary diseases:	240	70.6
Benign hypertrophy of the prostate	120	
Prostatitis	35	
Carcinoma of the prostate	18	
Carcinoma of the bladder	11	
Renal and urethral stones	11	
Miscellaneous: carcinoma of the kidney, pyelonephritis, stricture, tumors of the bladder, cystitis, etc.	45	
Hypertrophic arthritis	20	5.9
Cholecystitis with and without stones	10	2.9
Arteriosclerosis	13	3.9
Miscellaneous: pulmonary tuberculosis, latent syphilis, diabetes, myocardial degeneration, carcinoma of the stomach, etc.	57	16.7
Total	340	

Senescent arthritis occurs usually in persons beyond middle age, is generally confined to the distal joints of the hands as Heberden's nodes or to the spine and knee. The bony changes are almost always hypertrophic. This type is usually accompanied by mild hypertension, arteriosclerosis and other evidences of senescence.

Traumatic arthritis, acute or chronic, may be a periartthritis affecting only the soft tissues, or also the bone, in which case the bony changes are usually hypertrophic. Examples of this are "baseball fingers" and "static arthritis" such as are found in obese patients.

It will be seen, therefore, that hypertrophic bony changes are not confined to any one causative type of arthritis but may occur in several

different types, although the term hypertrophic arthritis is often used to mean exclusively a purely senescent or metabolic and not infectious form of the disease

The pathologic change seen in hypertrophic arthritis is described by Goldthwait as a proliferation of the edges of the articular cartilage, with subsequent ossification and extension of the process into the ligaments originating nearby

In elderly persons, such as those under consideration in this series, hypertrophic arthritis may well be due not to one factor alone but to a combination of factors. An analysis of possible causative factors has been made, foci of infection have been sought, chronic trauma, especially in cases of obesity, has been considered, and senescence has been determined by other evidences

That infection, slight or severe, may play some rôle in the etiology of the type of arthritis under discussion is generally agreed, although the degree and manner of its elucidation are sometimes difficult to determine. Even in cases which at first seem independent of infection there are good reasons for thinking that the microbe factor is contributory. Ely⁵ believes that the disease is primarily infectious and that "it is almost exclusively in persons whose alveolar processes have had abscesses at the roots of their dead teeth." Horder⁶ believes that the key to success in treating patients with arthritis is given by a full consideration of all the etiologic factors involved. The etiologic factors are various, and in the great majority of cases, if not in all, there is more than one factor. In such cases, the more accurately the value of the particular factor is estimated and dealt with, the better will be the response to treatment.

The 500 cases were considered from the standpoint of focal infection, the possible and apparent foci being teeth, tonsils and prostate. On account of controversial opinion regarding the intestine as a focus, a consideration of it as such was omitted. Teeth were considered as possible foci only when dental roentgenograms, showing periapical rarefaction, had been made and recorded, tonsils only when close inspection had been made and pus had been expressed, or when the laryngologist had reported that the tonsil was definitely septic, and the prostate only after microscopic examination of the prostatic fluid. Some of the prostates investigated showed no evidence of infection on the first examination, but from three to five days later, following a provocative test, a large number of pus cells were found in the secretion.

5 Ely, L. W. The Second Great Type of Chronic Arthritis in Its Relation to Industrial Accident Cases, California and West Med 22 260, 1924

6 Horder, Thomas. Discussion on Treatment of Chronic Arthritis, Brit M J 2 633, 1925

Ninety-four (58 per cent) of the women and 178 (52 per cent) of the men were referred for investigation of foci. Therefore, in discussing the incidence of focal infection, computation is necessarily limited to those cases receiving consideration from that standpoint. Of the sixty-two women who were referred for dental examination, fifty (80 per cent) showed periapical infection, and of the 125 men referred, ninety (72 per cent) showed similar involvement. Ten (15 per cent) of sixty-seven women and twenty-eight (20 per cent) of 138 men whose noses and throats were examined showed definite tonsillar sepsis. Other reports on the condition of the tonsils examined were given in thirty-nine of the women and in 111 of the men. Thirty-nine men were referred for prostatic investigation, of whom thirty (77 per cent) showed definite prostatic infection.

Besides the patients showing periapical involvement, there were nine women and twenty-eight men whose dental examination revealed pyorrhea without periapical infection. Therefore, if in addition to the patients with definite infection at the apexes, those showing pyorrhea alone are added, twenty-eight men and nine women, the proportion of dental infection is raised from 72 to 94 per cent in the men and from 80 to 95 per cent in the women. Eleven women and thirteen men had had all teeth extracted previously, presumably on account of infection, and, although they cannot be included in this computation since they were not referred for dental roentgenograms, they serve to increase the possible percentage of cases in which teeth may be considered as foci.

I have already mentioned other reports on the tonsillar conditions, of which thirty-nine were given in the cases of women and 111 in those of men. The determination of infectious potentialities of a tonsil by inspection is not always accurate, and doubtless many real foci are included in those cases not reported as definitely septic. C. H. Mayo⁷ has often emphasized that it is not always the large red tonsil that is most to be feared, that the small shriveled one which has lost the power to react against and localize its infection and harbors it in a crypt, sealed away from the exterior, is a source of danger. Twenty-three men and nineteen women gave histories of recurring attacks of tonsillitis or of having undergone tonsillectomy previously. In a certain percentage of these cases it might also reasonably be assumed that the tonsils had been active foci. Therefore it becomes apparent that although but 20 per cent of the men and 15 per cent of the women who underwent tonsillar examination gave definite evidences of septic tonsils these percentages might well be considerably increased speculatively. At least, if this more or less indeterminate group were considered.

7 Mayo, C. H., quoted by Hench, P. S. The Systemic Nature of Chronic Infectious Arthritis. *Atlantic M. J.* 28: 425, 1925.

Von Lackum and Holloway,⁸ of the Mayo Clinic, have reported several cases of primarily infectious arthritis of the spine, as well as some of this type under discussion, in which relief or amelioration of symptoms referable to the spinal condition was obtained through treatment of the inflamed prostate, so that now, in all cases of arthritis of the spine producing symptoms, it is customary to make a thorough examination of the prostate. Seventy and nine-tenths per cent of the patients of this series who had incidental spondylitis had some form of prostatic disease, as has been noted, including all forms encountered in the diagnoses. However, of the entire group of 340 men, the diagnosis of prostatitis was made in only forty-five cases (13.2 per cent). Intensive investigation of the prostate in thirty-nine revealed that thirty (77 per cent) had definite prostatic infection. I shall not venture even to intimate that this large incidence of pathologic conditions of the prostate may indicate that prostatic disease is an etiologic factor in the development of this type of arthritis, but it is a most interesting coincidence that the incidence of disease of the prostate in 360 cases was 70.9 per cent, and the occurrence of hypertrophic arthritis of the spine in more than 1,400 cases was 67 per cent. They are probably merely parallel manifestations of approaching age. In any other series of men over 50 a large proportion would be observed to have prostatic disease.

Under a discussion of possible etiology various forms of chronic trauma, including that associated with obesity, must be considered, and therefore an analysis was made of the frequency of occurrence of obesity. All patients who weighed more than 200 pounds (90 Kg.) were included in the obese group, also a few who weighed less, but were of short stature (table 7). The lightest patient weighed 160 pounds (72.6 Kg.), and was 5 feet 2 inches (157.5 cm.) tall. Only a small percentage of the patients were obese.

As mentioned before, certain forms of arthritis or osteo-arthritis seem to be essentially accompaniments of middle and late life and manifestations of approaching old age. According to Fisher,⁹ in the hieroglyphic writings "the determination of old age was the figure of an old man crippled with arthritis." Therefore I made note of "other evidences of senescence" in the case histories analyzed (table 8). Under one group I have listed the evidences of senile retrogressive change apart from the hypertrophy of the prostate in order that the comparison between the sexes might be less disproportionate. The evidences consisted of those

8 Von Lackum, W. H., and Holloway, J. K. Chronic Prostatitis with Special Reference to Its Focal Aspects, *M. J. and Rec.* **122**: 23 and 64, 1925.

9 Fisher, A. G. T. A Contribution to the Pathology and Etiology of Osteo-arthritis with Observations Upon the Principles Underlying Its Surgical Treatment, *Brit. J. Surg.* **10**: 52, 1922.

observations, encountered in the course of the average clinical examination, which betoken old age, palpable sclerosis of peripheral vessels, sclerosis of retinal arteries as seen with the ophthalmoscope, coronary sclerosis as suspected from the anamnesis, arcus senilis and the general appearance of the patient, such as one who was described as a "wizened up old man"

About one fourth to one third of the patients, therefore, showed other evidences of senescence. It is my belief that the condition "incidental hypertrophic arthritis" of the spine, as I have chosen to term it, is in no small degree a degenerative or senescent type, especially in men. Its presence in two thirds of 1,415 men more than 50 years of age would seem to support such a contention. Whether it is referred to as metabolic or traumatic or as due to the stress and strain of life is of little

TABLE 7—*Incidence of Obesity among Five Hundred Patients with Hypertrophic Arthritis of the Spine*

	Total Cases	Obesity	
		Cases	Per Cent
Men	340	37	10.9
Women	160	31	19.4

TABLE 8—*Evidences of Senescence Associated with Arthritis*

	Total Cases	Including Hyperprostate in Men		Excluding Hyperprostate in Men	
		Cases	Per Cent	Cases	Per Cent
Men	340	241	71.0	110	22.3
Women	160	39			24.3

moment, for fundamentally retrogressive metabolism and trauma are but different factors in the same process, and so these other evidences of senescence are interesting accompaniments. Fisher¹⁰ noted arteriosclerosis in the vessels of the synovial membrane, but considered the change in the vessels as merely coincidental. He believes that arteriosclerosis is inflammatory in origin, and therefore attributes the same cause to hypertrophic arthritis. In the cases reported by Swett,¹¹ arteriosclerosis and hypertrophic arthritis coexisted, and he considered the etiology of both to be the same. Peripheral and coronary sclerosis, arcus senilis, gray hair, hypertrophy of the prostate or atrophy of the uterus and senile vaginitis with senile tremors, the stooped posture and hypertrophic arthritis form a decisive clinical picture of the senescent person.

10 Fisher, A. G. T. The Nature of the So called Rheumatoid Arthritis and Osteo-arthritis, *Brit. M. J.* 2: 102, 1923.

11 Swett, P. P. The Association of Arterial Hypertension and Chronic Arthritis, *Am. J. Orthop. Surg.* 15: 635, 1917.

Why the incidence of the arthritis should be 67 per cent in men and only 40 per cent in women I cannot explain. Nor can I give a reason for the frequency of Heberden's nodes in women and their rarity in men, or why so relatively few women have angina pectoris. Allbutt¹² says that hospital records show that the proportion of men to women with arteriosclerosis is 3 to 1. His experience in private practice, however, does not substantiate this; he believes that the difference between the sexes in this liability, "at any rate to the descending kind," is inconsiderable. If arteriosclerosis is greater in men it may be considered a factor or rather as an indication that phenomena of senescence are more apparent in men.

However, if it is possible that a focus of infection in the prostate in cases of hypertrophic arthritis has a particular affinity for the spine, in view of the great number of pathologic conditions of the prostate in this series, the difference in incidence might be thus partially explained. It is interesting to note in this connection that carcinoma of the prostate rarely metastasizes to regions other than the lumbosacral spine. But as the prostate was investigated as a possible focus in only thirty-nine of the 340 men, and as 77 per cent of this group showed definite infection, the relative importance of prostatitis as an etiologic factor in this series can be only surmised, not conclusively stated.

Furthermore, to such possible etiologic factors as trauma, men are much more vulnerable than women, due to their greater exposure. Henderson¹³ has noted that hypertrophic arthritis of the spine is common in laboring men over 50. The counterpart of this is in the relative rarity of arthritis of the spine in women just referred to, while they have the marked preponderance of Heberden's nodes. The latter might be explained on the basis of mild chronic trauma incident to woman's "handiwork." Ely believes, though, that trauma is the cause of symptoms but not of the disease itself, that is, that it acts by spraining a joint already damaged by disease.

The practical application of the observations in this department concerns itself, therefore, with a rational therapeutic point of view and gives a basis for the development of certain principles of conservative treatment when considering the observation of such "incidental arthritis." If two thirds of the men past the age of 50 have demonstrable hypertrophic arthritis of the spine, and if of this large majority relatively few give symptoms definitely due to the disease process, the clinician's attitude on encountering such a case should be one of conservatism. To subject a patient of 60 to an extraction of teeth or tonsillectomy or other surgical intervention for focal infection solely on the basis of a positive

12 Allbutt, T. C. *Diseases of the Arteries, Including Angina Pectoris*. London, The Macmillan Company, 1915, vol. 1, p. 534.

13 Henderson, M. S. Personal communication.

roentgenogram of hypertrophic arthritis of the spine with only mild symptoms, is hardly advisable, to say the least. In other words this may be considered in the nature of a basis for a more rational and conservative consideration of the senescent and arthritic patient. Severe and disabling symptoms or evidences of a definitely progressive type of arthritis would justify more radical procedures. Such cases are most infrequent, however, and in the vast majority of them reassurance only should be necessary.

A second practical consideration is the medicolegal aspect especially in reference to cases resulting from industrial accidents, a point which Ely has emphasized. A man wrenches or twists his back while at work and complains of pain and then of disability. Roentgenograms show the characteristic lipping and spurring of hypertrophic arthritis and when the case is called for adjudication the question at issue is whether the injury is responsible for the arthritic changes shown in the roentgenogram. To grant this would be to deny the rôle attributed to the factors here considered—infection and the metabolic and senescent phenomena. That trauma may play some part in the etiology of hypertrophic arthritis is true, but by the term trauma as I have used it, is meant long-continued irritation of mild or moderate degree. To these factors is now added the fact that two thirds of the cases of this particular type of arthritis are found incidentally in patients undergoing investigation for complaints not germane to this particular condition. Therefore, the improbability of one single injury's being responsible for the observations of hypertrophic arthritis is obvious.

SUMMARY AND CONCLUSIONS

Apparently this "incidental" hypertrophic arthritis of the spine is the result of a combination of factors and not of any one factor. Infection plays a rôle, as indicated by the presence of foci in a fairly high percentage of cases. Chronic trauma is also a factor particularly in the obese group, presumably with exposure to irritation. Senescent or retrogressive metabolic changes are important causes.

If there are no symptoms treatment is unnecessary. With moderate symptoms conservative treatment is indicated. This would include primarily the total procedures of baking and massage and graded exercise. The conservative consideration of the removal of foci is then justified. Whenever possible the element of trauma should be minimized especially in the obese group by reducing the weight or by other means.

In a series of 2090 patients more than 50 years of age for whom roentgenograms of the kidneys, ureters and bladder were taken during 1925, 40 per cent of the women and 67 per cent of the men showed hypertrophic arthritis of the spine, which condition I have designated as incidental hypertrophic arthritis of the spine.

The case histories of 160 women and 340 men of the group with arthritis were analyzed in detail. On account of the nature of the group chosen, the predominating type of chief complaint was genito-urinary, as were also the primary diagnoses. Of the men, 70.9 per cent showed diseased prostates. Seventy-four per cent of the men and 61.3 per cent of the women were without any complaint whatsoever of the various types of "rheumatic," neuromuscular and arthritic pains.

Of the women whose teeth were investigated as possible foci, 80 per cent had periapical infection, including those with pyorrhea, 95 per cent had dental sepsis. Of the men, 72 per cent had periapical infection, including those with pyorrhea, 94 per cent had dental sepsis. Of those undergoing thorough examination of the tonsils, 15 per cent of the women and 20 per cent of the men showed definite tonsillar sepsis, 75 per cent of thirty-nine men referred for examination of the prostate had definite infection.

The traumatic factor in the etiology is partially illustrated by the presence of obesity, in which the assumption of chronic trauma can be made in 24 per cent of the men and in 33 per cent of the women.

The degenerative or senescent nature of this "incidental" arthritis is shown by other evidences of senescence in 71 per cent of the men, including hypertrophy of the prostate, and in 32.3 per cent excluding this condition. Such evidences were present in 32.3 per cent of the women.

In view of the high incidence in persons beyond the age of 50, especially in men, of hypertrophic arthritis of the spine, which is without symptoms in a majority of patients, a plea is made for conservative consideration, advice and treatment in such cases.

The improbability that a single accident or injury is responsible for the development of hypertrophic arthritis of the spine is obvious.

A REVIEW OF UROLOGIC SURGERY

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KIDNEY

Experimental Surgery—Perlmann and Kautz¹ report on resection of the kidney and transplantation of hemostatic tissue Bertl, in 1921, collected ninety-five cases of resection of the kidney, seventy-four patients were cured, seven were not cured, seven died, and in seven cases secondary nephrectomy was performed Tuffier was the first to show, by animal experimentation, how small a portion of renal substance is necessary to support life For animals, 15 Gm for each kilogram of body weight is sufficient, for man from 80 to 150 Gm is necessary (Kummell)

Four groups of experiments were performed In the first group from one fourth to one third of one kidney was resected, and the parenchymal wound packed with muscle or fat tissue From six to twenty-seven days later, the opposite kidney was removed Later the dogs were killed, and the resected kidney examined In the second group, nephrectomy was performed first and resection at the same time In the fourth group one kidney was removed and the opposite kidney was partially resected simultaneously

One dog in group 3, in which the upper third of each kidney had been simultaneously resected died from uremia three days after operation Both the dogs in group 4 in which partial resection and nephrectomy were simultaneously performed died one ten days after operation from renal insufficiency the second twenty-four hours after operation The other animals in which the operations on the two kidneys were performed at different times from one to three weeks apart remained alive until killed for an examination of the site of renal resection

¹ Perlmann S, and Kautz Z
20 595 1926

Bayle² carried out a study on compensatory renal hypertrophy in rabbits after unilateral nephrectomy. The remaining kidney was examined at varying periods. Comparative studies of the two kidneys were made in regard to volume, weight, dimension and histologic structure. In twenty-six of twenty-eight rabbits the remaining kidney was greater in weight and volume than the kidney first removed. The increase in weight and volume reached its maximum and terminated at about the forty-fifth day. In no case did the remaining kidney equal twice the weight of the other kidney, however, it usually increased from 60 to 70 per cent. There is not an exact parallelism between the hypertrophy and the increase in renal function, the augmented function is attained rapidly, the hypertrophy slowly.

The compensatory hypertrophy is produced by an increase in the volume of the elements already present in the kidney, not by the formation of new tubules and glomeruli. The width of the renal cortex of the hypertrophied kidney is double that of the other, and the surface of the hypertrophied glomeruli is correspondingly augmented. The diameter of the tubules is also somewhat larger than the diameter of the tubules of healthy kidneys. Bayle concludes that in healthy animals the combined phenomena of hypertrophy and cellular hyperplasia in the remaining kidney compensate exactly for the loss of renal secreting tissue due to unilateral nephrectomy.

Carson and Goldstein,³ in a study of experimental nephrotomy in dogs with only one kidney, found that dogs killed within forty days after nephrotomy showed no definite change in the size of the organ. However, in those killed after forty days, it showed some decrease in size after nephrotomy. Microscopic changes in the single kidneys were similar to those in dogs with the other kidney normal. In order to encourage destruction of the kidney, sutures were not used after nephrotomy.

Magoun studied the functional results of nephrotomy when sutures were employed, and was able to demonstrate a definite relationship between renal cell destruction and renal function, in other words, when much renal tissue was destroyed, renal function was reduced accordingly. Since microscopic study in Carson and Goldstein's series revealed a minimal destruction of renal tissue, even when only a single kidney remained, one can conclude that the function should be reduced only slightly.

These authors concluded that single or multiple nephrotomies without suture in dogs with a single kidney is a safe procedure, that

² Bayle Henri. *L'hypertrophie compensatrice du rein*, Paris med **32** 121, 1926.

³ Carson, W. J., and Goldstein, A. E. Experimental Nephrotomies. III. Nephrotomy without Sutures, in Dogs with Single Kidneys, *J Urol* **15**:505, 1926.

nephrolithotomy without suture in dogs is successful, and that histologic studies of nephrotomized kidneys without suture demonstrate a minimal destruction of renal tissue

Andler ⁴ states that the frequent occurrence of accessory renal vessels is due to the persistence of embryologic structures. Accessory vessels to the lower pole may cause stasis in the renal pelvis. The presence of these vessels and hydronephrosis does not always imply a simple relationship. In a strict sense they are not the cause of hydronephrosis, the vessels becoming causative agents only under certain conditions. The renal pelvis or the upper ureter can come in contact with accessory vessels, either by dislocation of the kidney or dilatation of the renal pelvis and ureter. With marked dilatation of the renal pelvis, a valve is formed at the ureteropelvic juncture, which may cause definite obstruction. Pyelographic and functional studies of the kidney are indispensable for a diagnosis which should be determined as early as possible.

The best treatment is early nephropexy with severance of the accessory vessels. The latter will not have unfavorable consequences. If a valve formation is present, it should be remedied by a plastic operation if possible, otherwise nephrectomy should be performed. Conservative surgical intervention is indicated for bilateral conditions or when the opposite kidney is subject to some disease. Infected hydronephrosis is a contraindication for conservative surgical intervention when the condition is unilateral.

[Ed. NOTE—The severance of accessory renal vessels is not always accomplished without harm to the kidney. The experimental work of Belt and Joelson ⁵ clearly showed that severance of a renal arterial branch causes necrosis of the area supplied by that vessel with, as an end-result, a depressed stellate scar equal in area to the region supplied by the ligated branch. The magnitude of such an area depends directly on the size of the ligated vessel. While this necrosis may not be extensive enough to produce clinical evidence of renal insufficiency, it definitely decreases the amount of renal reserve tissue, for restoration of function in such areas is revealed through their work to be anatomically impossible. When vessels of large size bridle the ureter and cause hydronephrosis, Quinby ⁶ has advocated free division of the ureter followed by its reimplantation into the most advantageous position of the pelvis away from the vessel. It must be remembered that anomalous conditions are frequently bilateral and hence there remains a potential source of similar

4 Andler, Rudolph. Neue Erfahrungen über die pathologische Bedeutung akzessorischer Nierengefäße. *Ztschr. f. urol. Chir.* **19**: 305, 1926.

5 Belt, A. E. and Joelson, J. I. The Effect of Ligation of Branches of the Renal Artery. *Arch. Surg.* **10**: 117 (Jan.) 1925.

6 Quinby, W. C. Hydronephrosis. *Tr. Am. A. Genito-Urin. Surg.* **15**: 43, 1922.

trouble on the opposite side, even in those cases in which it has as yet given no clinical evidence of its presence. On this account the procedure of choice is one which will result in the least destruction of renal tissue.]

Surgical Treatment in Nephritis—Damski⁷ publishes his personal experience with cases of nephritis of different types in which surgical intervention was necessary, to which he adds 110 cases of other authors. He draws the following conclusions. In cases of unilateral hematogenous nephritis, the diseased kidney should be exposed and radically operated on according to the degree of its destruction, even nephrectomy being performed at times. In ascending nephritis, the treatment should be expectant, except in serious cases with marked retention or infection, in which surgical measures are necessary, nephrectomy is contraindicated by the possible bilaterality of the lesions. In hemorrhagic, painful nephritis, in which category most of the cases of essential hematuria should be placed, operation is indicated, the most satisfactory operation is decapsulation, with nephropexy in cases of nephroptosis. Theoretically, in toxic nephrosis, especially that produced by sublimate, decapsulation should be performed, but in fact it does not produce a favorable result, as the toxic process involves not only both kidneys, but also the digestive tract. Damski agrees with most other authors in saying that in cases of chronic interstitial nephritis, mainly acute or subacute nephritis with oliguria, or anuria with edema, or serious uremia, the treatment should be decapsulation, cure has never been observed, but the amelioration may be of long duration. It is not in our power to influence the sclerotic or cirrhotic processes of glomerulonephritis, with or without signs of nephrosis. One of the author's cases proves also that decapsulation is of no value, and even harmful, in cases of advanced chronic nephritis with cirrhosis and arterial hypertension.

Hydronephrosis—Caulk⁸ states that the trend of modern renal surgery is toward conservatism, and that as a result many kidneys that would have been removed have been left to function. He reports a case of resection of a stricture of the superior renal pelvis for the relief of partial hydronephrosis. At operation it was noticed that entrance from the true pelvis to the upper superior part was markedly constricted. Partial nephrotomy was performed over this region in the upper part of the kidney, the renal substance being opened down into its pelvis. The upper part was moderately dilated, but still retained healthy cortical substance. It was impossible to enter the upper pelvis from below because of a dense scar. This mass of scar tissue was exposed and resected until the pelvis from below would admit one finger. A rubber

⁷ Damski, A. Sur le traitement chirurgical des nephrites, *J. d'urolog.* **21** 203, 1926.

⁸ Caulk, J. R. Resection of Stricture of the Superior Renal Pelvis for Relief of Partial Hydronephrosis, *Surg. Gynec. Obst.* **43** 279, 1926.

tube was inserted through the incision which had been made through the renal tissue, through the renal pelvis, and the resected area down to the true pelvis. Recovery was uneventful, and pyelograms show that the renal pelvis fills and that there is no retention in it.

Anomalies—Boss⁹ enumerates the factors in the diagnostic determination of the presence of horseshoe kidney. Frequently the condition is associated with defects of the general constitution such as psychic impairment, physical developmental anomalies in other organs or a "hypoplastic lymphatic development."

Symptoms due to the pressure of the fused kidney on other organs, or pain from pressure of a broad isthmus on the vertebral column or aorta are sometimes suggestive in the diagnosis. Inspection and percussion as a rule give little positive information. Occasionally tumor and rarely, stone may be felt in one half of a horseshoe kidney. The Schreiber-Seelig palpation albuminuria test may be of value.

In themselves cystoscopy and chromocystoscopy are of little diagnostic worth, but the introduction of opaque catheters and subsequent roentgenography with pyelometriography are of the greatest importance. When the catheters stop at a relatively low level on each side, horseshoe kidney is to be considered a possibility.

The direct roentgenogram is of value according to Voorhoeve in that it may demonstrate the following features: a vertical position of both kidneys, the inner edge running parallel to the vertebral column, a median displacement of both kidneys (the distance between the median edge of the kidney and the vertebral column is abnormally small), bilateral ptosis of the kidneys, immobility of the kidneys in a mediolateral direction, while mobility in an axial direction can be determined, apparent displacement of the lower renal pole in relation to the spinal column, and visibility of the connecting isthmus. Seldom are all of these roentgenographic features present. The abnormal roentgenographic relation of the colon to the low and medial horseshoe kidney may be of diagnostic significance especially if the stone has a long axis which is not to its position with reference to the ribs and spinal column may be of diagnostic significance especially if the stone has a long axis which is not to its position with reference to the ribs and spinal column.

By far the best and most positive information is revealed by pyelometriography. Usually the renal poles are displaced so that the lower kidneys tend to converge usually below. Again the insertion of the meter is usually placed at in monidous point often below the level of one kidney to the other in such a way that the connecting bar is better localized for operative attack.

Certain features noted at operation are worthy of mention the peritoneal fold extends far laterally, the fatty capsule of the kidney is poorly developed, the renal fossa is shallow, the suprarenals are not superimposed on the upper pole, there is marked lobulation of the renal surface, and many adherent vessels are encountered. The site of the pelvis is usually on the anterior face of the kidney, thus making its approach for pyelotomy somewhat easier. The ureter may be flattened out over the isthmus. In case the kidney is to be saved after division of the isthmus, care should be taken that the ureter is freed and its proper course maintained by nephropexy.

[ED NOTE—The diagnostic features mentioned, aside from pyelography, are for the most part indeterminate and hardly to be relied on. Since the advent of urographic study in its various details much has been learned with regard to horseshoe kidney. Before this time the diagnosis usually was made at the operating table. With careful pyelograms, however, at the present day it is possible in most instances to establish the diagnosis and to determine the operative procedure to be followed.]

Schillings¹⁰ reports a case of heminephrectomy for pyonephrosis in a horseshoe kidney. He reviewed the reports of 108 cases of surgically treated horseshoe kidney. In only twenty-two was the diagnosis made before operation. In twenty cases there was no lesion, eighteen showed hydronephrosis, eleven, pyonephrosis, twelve, tuberculosis, thirty-two, stones, four, neoplasms, and three, cysts. There were two cases of nephritis and two of trauma to the kidney, one case was complicated with a fistula and one with a ureteral stone. Heminephrectomy was performed in fifty-two cases, eight patients died. Palliative operations were performed in thirty-seven cases, with death in four.

Haas¹¹ comments on the relative frequency of horseshoe kidney, more than 300 cases having been described. Usually, through the obstruction to the urinary outflow, the conditions for the development of hydronephrosis, pyonephrosis and calculus are present. The usually demonstrable abnormal course of the ureter over the inferior renal pole with its consequent compression is noteworthy in this connection.

Tumors in horseshoe kidney are rare. The few cases published are remarkable, as all but one (a cystic tumor in the isthmus) have occurred in the right division of the double kidney. Haas describes an unusual case in which the resected right side of a double kidney showed three different types of renal tumor. The patient was a woman, aged 45, who had suffered from hematuria, pain in the right side and fever at intervals for three and a half years. Shortly before she was admitted

¹⁰ Schillings. Le rein en fer a cheval, *abstr.*, *Ztschr. f. urol. Chir.* **19** 410, 1926.

¹¹ Haas, N. C. Tumoren in Hufeisenmieren, *Ztschr. f. Urol.* **19** 81, 1925.

to the hospital, a papilloma of the bladder had been removed by fulguration. Because of persistence of pain and a mass in the right side about the size of a child's head, the patient was admitted to the hospital. On cystoscopy a gaping right ureter from which blood came in a thick stream was noted. The left ureter revealed clear urine, and the function of the left side was normal. At operation the right kidney was found to belong to the horseshoe type and was resected at the isthmus. In the specimen removed a hypernephroma the size of a fist was found in the upper pole, an adenoma the size of an egg in the lower third and a small papilloma in the lower division of the pelvis. The pathologic differences between the tumors were verified microscopically.

[ED NOTE—The occurrence of several types of tumor in the same organ is rare, but is occasionally seen. When a large mass is noted in the region of the kidney associated with papilloma of the bladder, the possibility of papilloma of the renal pelvis being present must be borne in mind. The case described, in which three separate neoplastic entities were encountered in the same kidney, belongs in the realm of pathologic curiosities.]

Siedner¹² reports a case in a woman, aged 32, who complained of renal colic on the left side. There was diminished function in the left kidney. The pyelogram showed a second cup-shaped pelvis above the normal pelvis, with its own ureter which joined the ureter of the normal pelvis at an acute angle. At operation this ureter was transplanted to the pelvis of the normal kidney, since its opening appeared stenosed. Convalescence was uneventful, and the patient was free from pain three months later, at which time the renal function had increased.

Anomalies and Calculi—Harbitz¹³ notes that Motzfeldt in 1914 collected an enormous amount of material dealing with anomalies of the kidneys and ureters. Motzfeldt studied the reports of about 4,500 necropsies. Harbitz carried on a similar series of investigations studying 942 necropsies of infants and 2,336 others. From these two series of necropsies, 7,778 in all, the following features were determined:

There were 161 instances of renal or ureteral anomalies (about 2 per cent), twenty-two cases of renal aplasia, twenty-two of renal hypoplasia, eighteen of horseshoe kidney, nine of ectopic kidney, thirty-seven of double ureter, forty-eight of kinks or congenital valve formation in the ureters with congenital hydronephrosis and five of cystic kidney. The number of anomalies reported is too small, as single cases of ureteral abnormality may easily escape attention. In the opinion of Harbitz the number should probably run about 3 per cent for

12. Siedner: Zur Operation von Doppelnieren, *Ztschr. f. Urol.* 19: 62, 1925.

13. Harbitz: F. Ureteranomalien, *Nordiskt Medicinskt Samfundnings Arsskrift*, 1925, 1926, 1927, 1928, 1929, 1930, 1931, 1932, 1933, 1934, 1935 and 1936, *Ztschr. f. Urol.* 19: 70, 1925.

Concerning the general conditions predisposing to the formation of calculus, Haibitz feels that a metabolic diathesis plays a great rôle in the formation of urate and oxalate stones, while infection is the important factor in the formation of phosphate stones. In necropsy material urate stones were more commonly found, in contrast to what is seen in surgical cases. The oxalate stones are relatively small, have sharp edges and for that reason may be associated with hemorrhage more frequently than the others. Calcium carbonate stones occur infrequently. They are white and hard. Among the rarer stones Haibitz mentions, besides cystin calculi, one of indigo in a 7 year old child who had had indigo in the urine for a rather long time and had died of intestinal tuberculosis.

[ED NOTE—This is an unusually large series of cases from necropsy material, and is of some value from the standpoint of geographic pathology in that it comes from a Norwegian source. The frequency with which renal and ureteral anomalies occur varies in detail with every long list of pathologic specimens studied, but on the whole Haibitz' review corresponds fairly well to that of European and American writers. As regards the structure of stones, there is a great divergence of statistical opinion with every series of stones analyzed. Likewise the question as to whether urate and oxalate calculi are the product of increased excretion of their chemical constituents (a so-called metabolic diathesis) or are due to renal infection is debated, and, in spite of much experimental work during the last six years, must be considered unsettled.]

Nephrolithiasis—Karris¹⁴ states that nephrolithiasis may be diagnosed either by colic, renal bleeding and passage of stone or by roentgen-ray examination. In modern diagnosis the latter is sufficient. There has, however, been a certain percentage of cases of failure of the roentgen ray to cast a shadow, in European clinics this figure is from 3 to 5 per cent. American observers have placed it at from 10 to 15 per cent. Many of these stones have been made visible by pyelography.

Karris reports a case in a woman, aged 37, with pain in the region of the left kidney. A plain roentgenogram was negative. Pyelography revealed a stone in the left renal pelvis. Six months later, the plain roentgenogram gave a positive picture of the stone. Pyelotomy was performed. The stone was found to be composed of calcium oxalate and calcium phosphate. Karris believes that the lack of cementing substances was the cause of its failure to cast a shadow at an earlier date.

Marion¹⁵ demonstrates the advantage of ureteral catheterization in ureteral colic due to calculi. He states that the patient is usually

14 Karris, Z. Beitrag zur Klinik und Diagnostik der Strahlendurchlässigen Nierensteine, Ztschr f urol Chir 20 66 1926

15 Marion, G. De l'utilité du cathétérisme urétéral dans la colique néphrétique par lithase, Presse med 33 1043 1925

relieved as soon as a catheter passes the stone, and the pelvis empties. Marion is an ardent advocate of leaving the ureteral catheter in place, even for several days, but does not advise it in every case. He limits it usually to cases in which there is repeated colic without passage of the stone and accompanied by fever. In one of his cases a woman had attacks of severe right renal colic for three years. The last crisis was of three weeks' duration, but not accompanied by fever; it could be controlled only with morphine. The ureter was easily catheterized, and the pain was immediately relieved. The roentgenogram showed a stone the size of a cherry in the upper ureter. In a second case there was pain in the right ureteral region of twenty-five days' duration. The diagnosis lay between renal and gallbladder colic. Ureteral catheterization was carried out, an obstruction, which was overcome, was encountered 17 cm above the ureteral orifice. The pains ceased completely after several hours. The catheter was left in place for twenty-four hours. Oil injections were given. The roentgenogram showed a stone in the upper third of the ureter. Eight days later the stone was passed spontaneously. In a third case, chills, vomiting and other serious symptoms accompanied the colic. Ureteral catheterization revealed an obstruction 15 cm up, a small ureteral bougie was passed. There was moderate fever for ten days, after which a new attack of pain set in. Ureteral catheterization was again performed, and as the catheter was engaging the ureter, the stone fell into the bladder. Marion also believes in the use of belladonna in preference to morphine.

Renal Tuberculosis—Rovsing and Frode¹⁶ reviewed their cases of renal tuberculosis. 632 cases from 31 various hospitals, 78 of these cases were eliminated. Analyzing the remaining 554 cases they come to the following conclusions. Urinary tuberculosis occurs most frequently between the ages of 20 and 40, a little earlier in women than in men. The right kidney is more commonly affected especially in men. Renal tuberculosis at times shows itself macroscopically as a diffuse process, when there is but one focus, it is usually in the upper pole. In 85 per cent of cases there were macroscopic changes in the meter. Trauma and gonorrhea have no relationship to the occurrence of urogenital tuberculosis. In women it frequently occurs in association with pregnancy. The initial symptom of renal tuberculosis is usually dysuria (62 per cent), less frequently renal pain (25 per cent) and occasionally hematuria. However in the course of the entire disease hematuria occurs in 50 per cent of cases. Albuminuria is present in 11 per cent of cases, pyuria is practically always present. Bacilli of tuberculosis were found

16. Rovsing Thorhild and Frode Rydgard. Klin. urol. 1920, 117, 27. Die Tuberkulose der Harnwege. Bibliogr. u. Ztschr. urol. Chir. 19 415, 1926.

in 78 per cent of cases. After nephrectomy, 13 per cent of the patients died while in the hospital, 98 per cent of the patients died from tuberculosis, general or affecting the remaining kidney, 32 per cent of them from operative complications. Technically it was found important in nephrectomy that the ureter be entirely removed through a button-hole incision in the iliac fossa. Records showed that 62 per cent were well following nephrectomy. Death usually occurred within the first year after nephrectomy and was generally due to tuberculosis of the remaining kidney or other organs. Postoperative treatment is important, especially in lesions of the bladder, which were treated with irrigations of phenol solution if they did not heal spontaneously.

Hofmann¹⁷ describes a case in which the bladder showed tuberculous changes, and, by inoculation of animals, tuberculosis of the right kidney was demonstrated. The patient refused operation, went to Kissingen and was treated with sun baths, rest, artificial sunlight and injections of tuberculin. About a year later he came under observation on account of tuberculosis of the left epididymis. The urine, however, was completely clear, and cystoscopy revealed a normal bladder with none of the tuberculous changes previously seen in the wall of the bladder or at the right ureteral orifice. Ureteral catheters returned clear urine from both sides, which was negative on inoculation of animals. Orchidectomy and epididymectomy on the left side revealed the typical picture of tuberculosis in the parts removed.

Hofmann feels that the case mentioned shows the possibility of renal tuberculosis being cured by conservative medical treatment, at least in rare instances.

[ED. NOTE.—Such reports as that of Hofmann appear from time to time in the literature and are of more than passing interest in that urologists of the present day generally hold that spontaneous cure of renal tuberculosis does not occur, and that relief is to be sought only when surgical measures are applicable. The contention might be raised that in Hofmann's case the kidney which he considered sound is still tuberculous, the process having been walled off (corresponding to the closed parenchymatous or occluded type described by Halle, Zuckerkandl and Braasch) in such a way as to prevent the escape of bacilli or pus cells into the urinary stream.]

Falci¹⁸ states that renal tuberculosis is a more serious disease in children than in adults. Fifty cases of renal tuberculosis were observed in children. Fourteen cases became bilateral, twenty-five remained unilateral and eleven disappeared from observation. Four patients were

17 Hofmann, Willy. Ueber ein Fall von konservativ geheilter Nierentuberkulose, *Zentralbl f Chir* 52 1025, 1925.

18 Falci, Emilio. La tuberculose renale de l'enfant (frequence evolution pronostic) comparée a celle de l'adulte. *J d'uro* 20 300 1925.

between 1 and 6 years of age, eight between 7 and 12 years and forty between 13 and 18 years. There were twenty-six boys and twenty-four girls. In thirty-six cases (72 per cent) the lesion was unilateral and in fourteen (27 per cent) bilateral. In a series of 177 adults it was unilateral in 152 (85.8 per cent) and bilateral in twenty-five (14 per cent). From this it is seen that in children the disease is more frequently bilateral. Further analysis shows that with increase in age in children, the tendency toward bilateral disease decreases. In adults this also occurs up to the age of 50, after which there is a tendency toward marked diminution in the percentage of bilateral lesions. Five children with bilateral disease lived from one month to four years. Three of eight more cases were lost sight of and five are living but are in poor health. Of twenty-five patients operated on eleven (44 per cent) died, in four the condition became worse and in four it remained stationary, six (24 per cent) were cured. Death was usually caused by generalized tuberculosis. In adults the number of cures is equivalent to 50 per cent as against 24 per cent in children.

Pazzi¹⁹ notes the association of calcified retroperitoneal and mesenteric lymph nodes in cases of renal tuberculosis. Occasionally these may be confused with renal and ureteral calculi by their form, position and radiologic relationship. In one case of renal tuberculosis a small round shadow was found in the corresponding renal field. This was thought to be caused by calcified lymph nodes. Studies with the roentgen-ray catheter and pyelography did not clear the situation; in fact, two additional shadows were found in the region of the lower pole. On examination the removed kidney showed that these shadows were caused by areas of caseation in the kidney. In another case of renal tuberculosis in a man aged 45 there was a shadow in association with the kidney. It was impossible to determine whether this was a stone or a lymph node. All studies on the kidney gave negative results except to reveal tuberculosis of the corresponding kidney. Following nephrectomy, roentgenograms still showed the same shadow. In a third case with a specific history, all urologic studies for tuberculosis were negative. Nevertheless roentgenograms showed two small round shadows in the region of the left ureter. Further studies showed that these shadows lay outside of the ureter.

Hels²⁰ has gathered his material from 377 cases of resected ureters for renal tuberculosis in which there were definite records concerning the treatment of the ureter and the course of healing of the wound.

19. Pazzi, Ermanno. Gangli calcificati nella tubercolosi renale. *Ann. Chir. 12* 536, 1925 (abstr. *Ztschr. urol. Chir.* **19** 415, 1925).

20. Hels, Robert. Ueber die Technik der Nephrektomie bei Nierentuberkulose mit besonderer Berücksichtigung der Peritonitis. *Monatsschr. Chir.* **117** 258, 1925 (abstr. *Ztschr. urol. Chir.* **19** 415, 1925).

In forty-two cases the ureter was resected through an incision in the iliac fossa with healing by primary union in 78.5 per cent, ureteral fistula in 9.5 per cent and tuberculosis of the soft tissues in 2.5 per cent, in 219 cases in which the ureter was removed through the nephrectomy incision, healing by primary union occurred in 74 per cent, ureteral fistula in 5 per cent and tuberculosis of the soft tissues in 17 per cent, in 116 cases the ureter was buried, with primary union in only 49 per cent.

[ED. NOTE.—Thevenot states that primary ureterectomy for renal tuberculosis has been abandoned in France, since in many cases it is useless, or it aggravates the postoperative condition. Persson states that the best results are obtained by simple primary suture after nephrectomy. In sixty-two of sixty-four cases in which the ureter was ligated and dropped into the wound and primary suture carried out, the wound healed in two weeks. Whenever any infection occurred, the wound was usually drained for three or four days only.]

Walters of the Mayo Clinic reported on the disposal of the ureter in 282 cases of nephrectomy for tuberculosis, in all cases complete data were obtainable. Ligation of the ureter with catgut and sterilization of the cut end with the cautery seems to have been the most effective means of treating the tuberculous ureters in which there was not sufficient stricture to produce distention. In 48 per cent of these cases there was primary union of the incision before the patient was dismissed from observation. The incisions remained healed without subsequent drainage. Twenty-seven per cent of patients similarly treated, whose incisions were draining when they were dismissed (from three to five weeks after operation), report subsequent permanent healing of their wounds.

Another method used in the Mayo Clinic was suturing the cut end of the ureter to the margin of the skin at the lower angle of the incision. This allowed escape of the contents of the ureters to the outside without contamination of the wound. This method has now been practically discarded in the Clinic, and it is interesting to note by actual comparison of the various methods, used for a period of seven years, that this one is ineffective, as measured by primary healing of the wound. Walters states that the results of partial or complete ureterectomy with nephrectomy, as measured by healing of the wound and ultimate end-results in fourteen cases of stricture of the tuberculous ureter insufficient to produce obstruction and distention, do not warrant the employment of the procedure as a routine. The cases of demonstrable stricture and distention of tuberculous ureters obviously form a separate group, since the stricture forms a closed sac if it is distal to the cut end of the ureter. W. J. Mayo now removes all ureters with the kidney if the constricted ureter is distended to a point below the stricture. In the other cases he

clamps the ureter with a hemostat without separating it from its fatty sheath, in order not to disturb its circumferential circulation, divides it with the cautery and drops it back without a ligature, which he believes might act as a foreign body. After thorough hemostasis the incision is closed without drainage. After his study Walters concludes that following nephrectomy for primary renal tuberculosis the method of compression of the stem of the ureter, ligation with catgut and sterilization of the cut end by the cautery produces the best end-results as measured by primary healing of the wound. Improvement takes place in vesical symptoms and in general health independent of drainage of the wound in the ureter after nephrectomy.

Young²¹ states that uncomplicated cases of renal tuberculosis are rare, the bladder is involved in about 40 per cent and the genital tract in about 26 per cent of cases. Genito-urinary tuberculosis is only rarely seen in large tuberculosis sanatoriums, it was found in only sixty-five of 10,000 sanatorium cases. Genito-urinary involvement makes tuberculosis of the lungs infinitely more dangerous than when other regions are affected, such as the bones.

Young reviews 222 cases of tuberculosis of the genital tract. Of these the genital cases with renal involvement numbered 114, genital cases with doubtful renal involvement eight, genital cases without such involvement, 100. Of the 222 cases in which the genital tract was affected, the kidneys were free in only 100, showing again the marked interrelationship in the disease. The epididymis was involved in 175, the seminal vesicles in 185. The epididymis was affected alone in thirty-seven cases, whereas the seminal vesicles were affected alone in forty-seven, showing that epididymal tuberculosis alone is the rarest of all forms of genito-urinary tuberculosis. In 191 cases of tuberculous infection of the prostate gland, the kidney was involved in eighty-six, in 171 there was other genital involvement.

Young states that nephrectomy can almost always be performed through a curved low incision extraperitoneally. When the ureter is exposed, he thinks it is important to inject pure phenol into it to destroy as far as possible, the tuberculous process in the mucous membrane. He does not think it wise to try to remove the entire ureter. The whole ureter cannot possibly be removed and it is dangerous to leave the last inch of the tuberculous ureter, opening into a deep fresh peridiverting wound instead of being brought near to the surface in a fibrous tube. He almost never removes the ureter unless it is dilated and distended. He injects phenol ligates the ureter and then excises the kidney.

²¹ Young H. H. Tuberculosis of the Genital Tract. *Ann. Surg.*
 1. Michigan M. S. 25 171 1926.

As a basis for prognosis it was found that in the case of malignant cystadenoma the proportion of living to dead was 2 : 1, in papillary carcinoma with clear cells, 1 : 1, in adenocarcinoma with granular cells, 1 : 3, and in alveolar carcinoma, 1 : 7.

Extension of carcinoma into the renal vein has long been observed and metastasis to the lung, bones and liver is usually recognized as being brought about in this manner. Such involvement of the renal vein begins in the small vessels, as was shown in a case reported by Keyser and Foulds.²⁷ That venous involvement is of grave import is shown by the fact that, of forty-five patients whose renal veins were grossly involved with tumor, nine died in the hospital, twenty-two died subsequently, five remained untraced, and only nine are known to be alive. However, certain patients survive for a long time. Albrecht²⁸ discusses two patients, in whom neoplasm had invaded the renal veins, who were alive and well four and a half years, and twelve years, respectively, after operation. Hyman²⁹ mentions two patients alive and well three and a half years, and four and a half years after nephrectomy. In the Mayo Clinic series, four remained well for six years, one for seven, one for eight, one for twelve years, and one for fourteen years after operation. Judd and Scholl³⁰ reported an unusual example of a fatal embolus arising from adenocarcinoma of the kidney which involved the renal vein and the vena cava.

In studying the gross pathology, two factors stand out—the size and site of the tumor. The size of the tumor bears a distinct relationship to the postoperative results. This is also apparent in the high mortality among patients with tumors that had caused such extensive destruction by their growth that their original site could not be determined. Large tumors are not only more difficult to remove completely, but also show a greater tendency to perirenal and pelvic involvement. If the tumor is situated in the median portion of the kidney there is early evidence of its presence, and it is discovered while relatively small. There is a larger percentage of living patients in this group than in the group of patients with polar tumors.

Involvement of the renal pelvis or extension through the renal capsule indicates that the disease is well advanced and that the prognosis is bad. Mere encroachment on the renal pelvis without actual involvement does not affect the course of the disease adversely.]

27 Keyser, L. D. and Foulds, G. S. The Extension of Hypernephroma by Way of the Renal Vein, *J. Urol.* **7** 463, 1922.

28 Albrecht, Paul. Beiträge zur Klinik und pathologischen Anatomie der malignen Hypernephrome. *Arch. f. klin. Chir.* **77** 1073, 1905.

29 Hyman, A. Tumors of the Kidney, *Surg. Gynec. Obst.* **32** 216, 1921.

30 Judd, E. S., and Scholl, A. J. Thrombosis and Embolism Resulting from Renal Tumors. *J. A. M. A.* **82** 75 (Jan. 12) 1924.

Albrecht found metastatic involvement in eight of fourteen carefully traced patients, and noted pulmonary metastasis in all cases in which the disease was advanced. The average postoperative length of life in twenty-one patients, of the Mayo Clinic series who died from metastasis was less than three years.

Cases are recorded in the literature of patients who remained in perfect health for several years and then died from metastasis. Among the outstanding cases are those of Albrecht and Clairmont, in which the patients lived for seven and ten years, respectively, after operation and died later from metastasis.

Broster³¹ reports the case of a patient who remained well for nine years after nephrectomy by Thompson-Walker, and then suffered a spontaneous fracture of the femur, the result of secondary tumor. Cases like these make one doubt reports of cure in cases of hypernephroma. Certainly the three or five year series usually allowed in other types of malignancy is inadequate in renal tumors.

Tumor of the Renal Capsule—Haslinger³² states that the most common renal tumors are hypernephroma, carcinoma and sarcoma. Tumors of the capsule and perineal fat are noteworthy for their infrequency. They are rarely diagnosed preoperatively. In spite of the progress of urologic diagnosis, it is often impossible to ascertain whether a tumor is in the parenchyma or in the capsule. Infiltration to the adjacent organs confuses the diagnosis and makes excision extremely difficult.

Haslinger reports a case of a patient, aged 53, with a tumor in the region of the right kidney. She complained of gastric pressure, nausea, vomiting and belching. Cystoscopy and pyelography showed kinking of the right ureter with the kidney displaced downward and calcareous deposits along its outline. Exploratory operation revealed a tumor around the kidney involving the peritoneum and ascending colon. Death occurred twenty-four days after operation. At necropsy a tumor 25 cm. long, 12 cm. wide and 7 cm. thick was found. Pathologically it was of a mixed type showing mainly a fibrolipoma with lipoblasts. In cross section there was a vascularized polymorphocellular sarcoma. Throughout the tumor were deposits of bone.

In discussing these cases Haslinger states that tumors of the body of the kidney must be differentiated into connective tissue tumors of the renal capsule and those of the perineal fat layer. The former are more uncommon. Pathologically they are either paraneoplasms or mixed tumors undergoing malignant degeneration. In 1921 he reviewed cases of 165 such tumors and found 100 sarcomas.

31. Broster, I. R. A Case of Secondary Malignancy of the Femur Following Nephrectomy. *Spontaneous Fracture of the Femur*, **11**: 287, 1921, 1922.

32. Haslinger, Koh. *Urologische Chirurgie*, 1921.
Urol. Chir. **20**: 82, 1921.

20 per cent fibrolipomas, 10 per cent myolipomas, 10 per cent fibromyolipomas and 14 per cent sarcomas. Alexander considered heredity, congenital disposition, peripheral nervous disturbances and diseases of the thyroid and hypophysis as possible factors in the etiology. Birsch-Hirschfeld classified them as embryonic adenomas or sarcomatous glandular swellings. He believes that they originate in a part of the wolffian body which has continued to develop after birth. These tumors have also been designated as blastomas because often many connective tissue elements are present. Bone has often been found. Haslinger believes that these tumors may possibly be due to pressure on the renal artery or to bleeding in the renal capsule followed by organization. Muscle tissue has also been found. Because of the presence of the many and varied tissues, some observers have considered the tumors embryonic in type. Many are characteristic because of their large growth, ranging in weight sometimes from 30 to 60 pounds (13.6 to 27.2 Kg). There is a marked tendency to recur. The operative mortality is high, but the chief cause of death is from recurrence. Haslinger advises a transperitoneal approach and resection of all the perirenal fat. If possible, the tumor should be removed and the kidney left, if it is in good condition.

Tumor of the Renal Pelvis—Haslinger³³ notes that papillomatous tumors of the renal pelvis are rare, in spite of the numerous publications concerning them that have appeared in recent years. In sixteen years only two cases were found in his clinic, although during the same time 306 (0.65 per cent) kidneys had been operated on. The etiology is not clear, but hereditary disposition of the mucous membrane toward tumor formation, chronic irritation through pyelitis, calculi, chemical irritation and other causes are cited as possibilities. The literature shows that 50 per cent of the tumors undergo malignant degeneration and spread to the ureter and bladder. Diagnosis offers many difficulties. Because of the tendency of the tumors to spread and become malignant, the only treatment is nephro-ureterectomy. Haslinger reports two cases, in one of which there was a double ureter.

Interrenal Tumor—Gordon and Feldman³⁴ described an interesting retroperitoneal tumor. The situation is difficult to diagnose accurately unless urinary disturbances are associated. The possible conditions to be considered are the retroperitoneal lymphosarcomas, lipomas, fibromas and various tumor-like disturbances of development connected with the suprarenals, kidney or retroperitoneal cysts. The case of a woman, aged 60, is reported who had intermittent pain and swelling in the region of the left kidney for four years. The pain gradually became

33 Haslinger, Kolman. Die Zottengeschwulste des Nierenbeckens. *Ztschr f urol Chir* 20: 77, 1926.

34 Gordon, W. H., and Feldman, M. S. An Unusual Abdominal Neoplasm. Interrenal Rhabdomyoma, *Ann Clin Med* 3: 706, 1924-1925.

more severe and was associated with constipation and bloody stools. Operation revealed an extensive carcinoma which apparently involved the pancreas. Roentgen-ray treatment was instituted, but did not relieve her. Later, on cystoscopic examination, a provisional diagnosis of tumor of the left kidney was made. Dr. Hugh Cabot operated and found a large operable tumor resembling a retroperitoneal sarcoma, the source of which he was unable to determine. Further roentgen-ray treatment was given and finally to control the pain a cordotomy was performed. The patient continued to fail and died several months later.

At necropsy the tumor appeared to have originated at the junction of the celiac axis and the aorta. It involved the renal pelvis, left suprarenal, pancreas, aorta and adjacent tissues. When sectioned it resembled an ordinary myoma of the uterus. The diagnosis of various pathologists to whom tissue was submitted are substantially as follows: (1) leiomyosarcoma arising from the aortic wall with low grade of malignancy (P. F. Morse), (2) congenital interrenal rhabdomyoma, cellular and atypical in areas, to be called a rhabdomyosarcoma, of local malignancy only and arising primarily in a disturbance of development of the myotome (A. S. Warthin), (3) leiomyosarcoma (malignant leiomyoma) (B. Lucke), and (4) leiomyosarcoma (J. Ewing). In the final discussion the tumor was called a rhabdomyoma.

Clinically, rhabdomyomas are most often found in the genito-urinary tract. They usually grow slowly, but may undergo malignant changes and grow rapidly. In the differential diagnosis of retroperitoneal tumors the possibility of congenital disturbances of development in the form of interrenal teratomas genetically related to those of the kidney must be considered.

Renal Cyst—Begg³⁵ asserts that solitary hemorrhagic cysts of the kidney are rare, only about twelve cases being reported. These cysts are of the nature of partial hematonephrosis when the source of the bleeding remains active for a long time. In some instances the cyst may arise from an angioma of the renal parenchyma. Begg reports a case in which the lower pole of the kidney is entirely occupied by a cystic tumor 11 cm. in diameter. The wall of the cyst is completely fibrous and varies in thickness between 1 and 2.5 mm. On incision the tumor 250 cc. of dark fluid blood and curdy clot escaped. The internal lining of the cyst is smooth and glistening except where it is covered by a thin layer of fibrin and clot are adherent. No dilated veins and no arteries of the kidney are apparent in the wall of the cyst. The upper part of the kidney and renal pelvis is normal; the lower is absent. A slight constriction exists between the upper part of the cyst and the pelvis.

35. Begg, R. C. Solitary Hemorrhagic Cyst of the Kidney. *Ann. Surg.* 1926, 82: 102. This is a Case Originating in a Cystic Degeneration of the Kidney. 1926.

bristle can be passed. At two points bosses project externally. At the upper part the cyst is separated from the remainder of the kidney by its laminated fibrous wall, and the part of the kidney immediately adjacent to this appears to be pale and compressed. The internal measurements of the cyst are 9.2 cm. from above down, and 6.8 cm. in the other two diameters. The whole was covered by the fibrous capsule of the kidney, which passed without interruption into the capsule of the sound part of the organ.

Extrarenal Hypernephroma—Tyson³⁶ reports a case of hypernephroma of the gallbladder in a woman, aged 63. The gallbladder was removed, and the patient recovered from the operation. On section the gallbladder was a mass of growth. The histologic characters of the tumor were identical with those described as being typical of hypernephroma by Grawitz in 1883. No portion of gallbladder could be identified in the sections. But at one side there was a small portion of liver. The clear cells with distinct walls supported by a fibrous stroma could not be confused with those of any other neoplasm. Piney, who examined the tumor, said that the present tendency is to regard renal hypernephroma as being derived from altered renal cells, and there can be no doubt that true suprarenal rests in this organ are far from common, although the theory that hypernephromas grow from such structures would presuppose their comparatively frequent presence.

Suprarenal rests are extremely common in certain situations, for example, along the spermatic cord, in the broad ligament and on the under surface of the liver, but no record is available of such a structure in the wall of the gallbladder. Borst is still strongly of the opinion that the majority, if not all, hypernephromas are of suprarenal origin, and there is much to support this view, if it is accepted, the explanation of the genesis of the present tumor would not present insuperable difficulties. The neoplastic growth, either of suprarenal rest in the liver near the gallbladder or in the wall of the gallbladder, would well account for its occurrence.

Pyelonephritis—Caulk³⁷ reviewed 2,100 cases of renal infection, 1,191 occurred in adults and 909 in children. The relative frequency in male and female seems dependent on the period of life. In children, girls predominate 3:1. In this series there were 684 girls and 225 boys, in adults the proportion is almost 2:1. 755 were women and 436 were men. In 102 cases renal infection complicated pregnancy. With this contributing element eliminated the incidence is not strikingly different, about 33 per cent in favor of the female. In the latter period

³⁶ Tyson, Wilson. Hypernephroma of Gall-Bladder. Cholecystectomy, Brit J Surg **13**:757 1926.

³⁷ Caulk, J. R. Pyelonephritis. Its Incidence, Engendering Elements and Impelling Influences. J Urol **16**:117 1926.

of life, between the ages of 50 and 80 when renal infections resulting from obstructions of the lower urinary tract are so frequent in men the proportion in men and women is more nearly equal being 163:201.

The most important feature not only in the production but in the perpetuation of renal infection is stasis. It may be the result of pre-existing pathologic processes within the urinary tract or secondary to some extrinsic influence particularly to pressure resulting from morbid processes in some of the other organs or tissues or it may be self-engendered or automatic and secondary to the infection from the kidney itself. The latter type is Caulk's impression of the fundamental feature in the foreground of so-called acute pyelonephritis which usually disappears spontaneously, but in many instances leaves its scar.

Opinion has varied relative to stasis resulting from pre-existing obstruction. If one should accept the work of Biedl and Krimm, Lammie and Abrams, Mayer, Heyn and others that a healthy kidney excretes bacteria, it would be perfectly easy to explain these infections as "filth in a pool" or the contamination of a stagnant pond but the work of Peirce, Scagholse, Sherrington, Dyke, and particularly that of Helmholtz, has shown definitely that bacteria are not excreted through a kidney unless the integrity of its secreting surface has been broken. Therefore, it must be a question of pressure and the effect exerted on the circulatory bed. Whatever the cause, the effect when once produced should be remedied as promptly as possible to protect against back pressure whether this is through the tubular system lymphatic or the venous channels, as Humm recently described the secreting surface should be protected from further invasion.

Levy-Drevfus³⁸ reports an unusual case of bilateral pyelonephritis complicated by severe hematuria. The hematuria which was profuse was the first symptom and had started three days previously. During the same period there had been dysuria and frequency which disappeared after forty-eight hours. The patient had diabetes, obstructive constipation and a cardiac lesion. Physical examination revealed no right kidney. Cystoscopic examination of the bladder gave negative results. Both ureters were catheterized following which severe hematuria and pain on the right side again occurred. After the first Roentgenograms of the kidneys were negative. Following the second ureteral catheterization a large amount of blood was voided from both kidneys as well as pus colored urine. The capacity of each pelvis was 9 cc. and the phenol-sulphonphthalein test showed retention of 22 per cent on the right and 21 per cent on the left. A cystostomy was performed.

³⁸ Levy-Drevfus, R. *Arch. Intern. Med.*, 1925, 35: 1025.
 1. Recovery of the patient was complete.
 2. The patient died on the 19th day of the disease.

nephritis was made. Several hours after the ureteral catheterization, the patient had a chill, increased temperature, thready pulse, profuse hematuria and frequency. She was given caffeine and camphor, and 1 Gm methenamine intravenously. The retention catheter was left in place for five days, during which time the urine became normal. The patient was placed on a milk and vegetable diet for five weeks, and the bladder was irrigated frequently. She recovered, and the urine was free from pus and bacteria.

[ED NOTE—This type of urinary infection is rare, but it has previously been described by Marion. The heavy renal bleeding may readily complicate the diagnosis, the high temperature is unusual and may be explained by the presence of the diabetes. The important points in the treatment of the case are the insertion of the retention catheter and frequent irrigations of the bladder.]

Dudgeon,³⁹ in a symposium on renal infections at the Royal Society of Medicine, classified the types of infection into (1) infections due to a special group of hemolytic bacilli, (2) infection due to *Bacillus coli*, (3) *Bacillus proteus* and (4) *Staphylococcus albus*.

The great differences between the special hemolytic bacillus infection and those due to *Bacillus coli* were that they ran a more acute course as a rule, and were of longer duration, that complete recovery usually occurred and the urine became free from the infective organism, and that there was hypersensitiveness to specific vaccines.

Colon bacilli infecting the urinary tract may be grouped into hemolytic and nonhemolytic strains. The hemolytic group accounted for about 70 per cent of cases in men and about 30 per cent in women, although the percentage was higher in women suffering from acute fever. With the nonhemolytic group the percentages among men and women were reversed. Rabbits were readily immunized by the hemolytic group, but often with great difficulty by the nonhemolytic.

Although from inexperience *Bacillus proteus* had been regarded as nonpathogenic to man, it is well to realize that it may give rise to acute infections, and the bacillus can then be recovered from the blood stream. The temperature in some proteus infections reaches a high level. The urine is alkaline, contains mucus and pus and often masses of triple phosphate with the mucus. Vaccine treatment has been found to be of definite value when the acute stage is over.

The presence of *Staphylococcus albus* in large numbers in the urine, together with pus, was, in the author's experience, invariably associated with the presence of a calculus.

³⁹ Dudgeon L. S., Lepper, Elizabeth, and Thomson-Walker, J. Discussion on Bacterial Infections of the Urinary Tract, Proc Roy Soc Med 18 43, 1925

Lepper,³⁹ after reviewing the literature concluded that in spite of apparently contradictory statements the following facts had been established: (1) It is comparatively easy to produce lesions in a kidney by injections of organisms either into the blood stream or into the ureter, provided some obstruction of the ureter is produced at that time, and (2) inflammatory changes of the substance of the kidney or its pelvis can be produced by the intravenous injection of bacilli alone without the presence of obstruction to the outflow of the urine; the occurrence of such lesions is, however, uncertain as is also the degree of severity and their localization.

Experiments were carried out by Lepper to produce an only slight lesion in order to determine why obstruction to the outflow of urine is so important. She found that in the experimental production of lesions in the kidney, obstruction of the ureter is important in bringing about dilatation of the pelvis and pressure on the veins which may result in extravasation of infected blood into the substance of the kidney and subsequently diffuse inflammatory changes throughout the kidney. Intravenous injection alone, however, acts by producing embolism of small arteries, especially those supplying the papilla; the lesions are localized, and much less severe than those produced by the extravasation of infected blood into the tissues, such as occurs after obstruction of the ureter.

Thomson-Walker⁴⁰ divides urinary infection into two groups: (1) infection in a urinary tract already the seat of disease such as stricture, enlarged prostate, growths in the bladder or stone, and (2) infection in a previously healthy urinary tract. In the present discussion, he deals only with the latter. He describes fully the symptoms and course of acute infections. The more obscure clinical cases in which the symptoms do not present themselves so clearly include those in which high temperature may be the only symptom and in which only examination of the urine will reveal the nature of the disease. This is more often seen in children. In other cases pain alone may be present or may be the most prominent symptom. The aching pain of pyelitis may be mistaken for appendicitis. Hematuria as an initial symptom may be puzzling. There is also a group of cases, fortunately a small one, in which the infection is cortical and in which the urine is sterile.

There are three common varieties of chronic cystitis: (1) recurrent pyelitis and cystitis, (2) chronic cystitis without pyelitis and (3) bacilluria with toxemia. The most common is the first, commonly *Bacillus coli*, which is normally present in the large intestine. Thomson-Walker has noted the frequency of infection of the large bowel in the course of abdominal surgery and has therefore recommended the administration of antibiotics to the

abdominal operations. In discussing treatment he reviews the use of alkalies, diuretics and urinary antiseptics. He cautions against the use of hexylresorcinol in cases in which chronic nephritis is associated. His remarks on the use of intravenous injections of drugs are disparaging. He approves of renal lavage in the chronic cases.

Feirer, Meader and Leonard⁴⁰ made a study of the drugfast character of organisms. They used cultures as follows: the Hopkins strain of *Bacillus typhosus*, a strain of *Bacillus coli* isolated from the stool of a typhoid carrier who had been taking hexylresorcinol for one year, a strain of *Bacillus coli* isolated from the stool of a normal adult, a strain of *Bacillus lactis aerogenes* isolated from the urine of a patient who had been taking hexylresorcinol for more than one year, and a strain of *Bacillus coli* isolated from the urine of a patient who had not taken any drug.

They investigated the development of the drugfast character in these strains to silver nitrate, mercurochrome 220-soluble, formaldehyde (to represent methenamine), acriflavine, hexylresorcinol and phenol.

It is clear that the resistance of certain organisms to the bacteriostatic influence of the drugs ordinarily employed in the treatment of urinary infections may be raised to a high degree, that this resistance is highly specific and that in acquiring it the strain may become much more sensitive to the action of certain other germicides. It was hoped that this investigation would result in an exact and explicit method of drug rotation so that the treatment of all these infections might be begun with a definite drug for the purpose of enhancing greatly the susceptibility of the offending organism to the action of another. While these experiments point definitely to principles which may have an important clinical bearing, the few cultures examined vary too widely in their reactions to these germicides to admit of sweeping conclusions.

The authors found that *Bacillus coli* and *Bacillus lactis aerogenes* may develop enormous resistance to the action of silver nitrate and mercurochrome-220 soluble when exposed in the test tube to concentrations of these germicides permitting growth. Under the same conditions these organisms may become from five to fourteen times more resistant to the bacteriostatic action of formaldehyde and acriflavine, but develop only a relatively slight tolerance to hexylresorcinol and phenol.

The drugfast character is highly specific. None of the thirty drugfast substrains showed increased tolerance to any of the germicides ordinarily employed in the treatment of urinary infections other than the particular one to which it had been exposed.

40 Feirer, W. A., Meader, P. D., and Leonard, V. Development of the Drug Fast Character in Vitro and Its Bearing upon Drug Rotation in the Management of Chronic Urinary Infections, *J. Urol.* 16:97, 1926.

The acquirement by bacteria of a specific drugfast character may be accompanied by a greatly increased sensitiveness to the action of other germicides, but this increased sensitiveness bears no relationship to the degree of drugfastness acquired. A substrain which has acquired great resistance to the action of a derivative of one of the heavy metals (mercurochrome) may show no marked increase in sensitiveness to other germicides, while the same cultures exposed to the action of a drug which does not lend itself to the development of more than a slight degree of the drugfast character (hexylresorcinol) may become much more sensitive to the action of other germicides.

While cultures exposed to the action of one germicide (hexylresorcinol) may develop substrains of much greater sensitiveness to the action of another (formaldehyde), the substrains of the same cultures developed by exposure to the action of the latter germicide may show no increased sensitiveness to the former. The authors suggest that the results of these experiments indicate a logical plan of drug rotation in the treatment of chronic urinary infections.

If treatment has not been given, hexylresorcinol should be administered by mouth for a period of from thirty to sixty days. Large doses should then be substituted, and silver nitrate solutions employed locally. Throughout this treatment the fluid intake should not be increased. If silver nitrate has been used persistently, hexylresorcinol or acriflavine should be administered by mouth, and acriflavine should be employed locally. If mercurochrome has been used persistently, the offending organism has probably developed an increased resistance to mercury. Hexylresorcinol or acriflavine should be administered by mouth to be followed after from thirty to sixty days by methenamine in large doses and silver nitrate locally. If methenamine has been used persistently, the organism may have developed increased sensitiveness to silver nitrate and this should be tried locally. If no improvement results, the rotation should be as indicated in an untreated patient.

If acriflavine has been used persistently, silver nitrate should be employed locally and methenamine or hexylresorcinol administered by mouth. If hexylresorcinol has been used persistently, large doses of methenamine should be substituted together with silver nitrate locally. If no improvement results, acriflavine should be administered by mouth for from thirty to sixty days to be followed by the use of methenamine and silver nitrate locally.

If these various rotations prove to be unsuccessful, the authors should be that arranged for in untreated patient. It should be noted in this connection that the highest percentage of cures was obtained in a series of chronic urinary infections was reported by the New York Hospital following the simultaneous use of hexylresorcinol by mouth and acriflavine locally. There is no doubt that the

advantage in this method, although it does not appear to be related to the development of the drugfast character

Any change from one drug to another should be sudden and complete, and there should be no interval of suspended treatment between the two. The drugfast character developed in the test tube is lost, to some extent at least, after a few days' cultivation of the organism in a drug-free environment, and its enhanced susceptibility to the action of other germicides may presumably become lessened in like degree under these circumstances

Perinephritic Abscess—Pugh⁴¹ reports two cases of perinephritic abscess, one in a girl aged 5, the other in a boy, aged 8. Both were successfully operated on under local anesthesia. Pugh concludes that perinephritic abscess formation, particularly that due to metastasis, is more common than is generally supposed. The history of infection and pain in the costovertebral angle in children suggests the condition. All doubtful cases should be studied thoroughly from a urologic standpoint and an exploratory operation performed, it can and should be performed under local anesthesia

41 Pugh, W. S. Perinephritic Abscess in Children, *Urol & Cutan Rev* 29:387, 1925

(To be continued)

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POSTOPERATIVE PULMONARY ATLECTASIS

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ing in 2,000 abdominal operations in 1914. In the same year, Elliott and Dingley⁴ reported eleven cases following abdominal operations.

During the period between 1918 and 1920, Bradford⁵ studied massive collapse in connection with war wounds.

Scrimger⁶ was the first to describe this condition in the American literature. In 1921, he reported seven postoperative cases, four of which followed appendectomy, two, hemorrhaphy, and one, hemorrhoidectomy.

In 1925, Scott⁷ reviewed all the reported cases of the postoperative variety and found sixty-four cases, to which he added four of his own. In September of the same year, Jackson and Lee⁸ demonstrated the relationship between massive atelectasis and plugging of the bronchi by foreign bodies or secretion, the removal of which leads to a gradual reinflation of the collapsed lung.

THEORY

Four theories have been evolved as a result of the observations and investigations conducted by various authors.

1 In 1908, Pasteur⁹ advanced the opinion that collapse of the wall of the chest, due to paralysis of the diaphragm and, probably, of the accessory respiratory muscles, was primary and that the collapse of the lung was secondary. Subsequent investigators, adhering to this original opinion, added the statement that any bronchial secretion which may be found is present merely as a result of diminished aeration and may aid the process. Bradford⁵ was a supporter of this idea. The observations of Sante¹⁰ do not support this theory.

2 Elliott and Dingley⁴ failed to obtain atelectasis in cats, when they produced hemiparalysis of the diaphragm and the respiratory musculature. They advanced the theory that atelectasis was produced as a result of diaphragmatic immobilization associated with bronchial obstruction, the alveolar air being absorbed by the circulating blood. Jackson and Lee⁸ and Tucker¹⁰ favor this explanation and maintain that obstruction alone, produced by inspissated mucus plugs, may cause atelectasis.

3 Briscoe¹¹ considered the atelectasis secondary to inflammation affecting the retroperitoneal portion of the diaphragm. This results in

4 Elliott, T. R., and Dingley, L. A. *Lancet* **1** 1305, 1914.

5 Bradford, Sir J. R. *Oxford Loose-Leaf Medicine* **2** 127, 1920.

6 Scrimger, F. A. C. *Surg Gynec Obst* **32** 486 (June) 1921.

7 Scott, W. J. M. *Postoperative Massive Collapse of Lung*, *Arch Surg*

10 **73** (Jan) 1925.

8 Pasteur, William. *Bradshaw Lecture*, Royal College of Physicians, 1908.

9 Sante, L. R. *Radiology* **8** 1 (Jan) 1927.

10 Tucker, Gabriel. *Surg Gynec Obst* **42** 743 1926.

11 Briscoe, J. C. *Quart J Med* **8** 293 1920.

a disturbance of the function of the diaphragm and the associated respiratory muscles on the involved side.

4 Bradford,⁵ although favoring the theory of Pasteur,³ suggested that the condition could be brought about by vagal stimulation affecting the constrictor mechanism of the bronchioles, but he could not offer any corroborative evidence. Scott⁷ favors this theory and considers that atelectasis is produced by means of a vasomotor mechanism, the atelectasis being primary and the bronchial obstruction secondary. A thick, tenacious mucus present in the bronchi due to the stimulation of a low grade infection is the cause of the obstruction. Sauer⁸ adds that the force of cohesion held the walls of the bronchioles in apposition, once they were approximated. Trout and Haver⁹ are of the opinion that anesthetics do not play a part in the production of this complication and also give support to the theory of Bradford.

The contralateral variety of atelectasis following slight trauma or fracture as noted by Bradford⁵ is best explained by the fourth theory. The experimental work of Carlson¹ has been cited as supportive of this theory. This author produced contraction and expansion of the lungs of certain amphibians by stimulation of the vagus and demonstrated the same effect by electrical and mechanical stimulation of per-

a mild bronchitis prior to operation develop an extraordinary degree of bronchorrhea postoperatively, even after spinal, local or gas anesthesia

(b) The cough reflex is in abeyance, due partly to the use of morphine and partly to the voluntary postoperative inhibition of muscular activity permitting accumulation of secretion

(c) When the obstruction is complete in any bronchus, the imprisoned air is absorbed by the circulating blood, and atelectasis ensues

In further support of our belief, the following facts are offered

1 Physical examination of patients immediately following operation and at various intervals thereafter has shown that atelectasis does not occur until several hours have elapsed. This argues against the sudden production of atelectasis by means of a reflex vagus mechanism and shows that time must elapse during which there is an accumulation of mucus leading to bronchial obstruction

2 In a number of instances, we have been able to anticipate the development of atelectasis in patients under anesthesia, who gave evidence of increased secretion in the respiratory tract. We have applied the term "wet patients" to these cases

3 The finding of mucus plugs by Jackson and Lee¹ in two cases at necropsy, and the demonstration of such plugs in vivo. Nearly all observers have noted the presence of mucopurulent expectoration

4 Reinflation of the atelectatic lung following bronchoscopic aspiration of the mucus, as described by Tucker¹⁰ and Manges¹⁵

5 Recurrence of atelectasis following reaccumulation of mucus in the bronchial tree, in amounts sufficient to produce obstruction. The cycle of secretion-obstruction-atelectasis-aspiration-reinflation has been completed seven times in one case, reported by Hearn and Clerf¹⁶. It would be difficult to explain this phenomenon on the basis of stimulation of the vagus

6 Atelectasis of mild degree may be produced in normal persons by placing them for a time on their right side. However, this differs from the postoperative form in that it disappears immediately on a deep inspiration, as shown by fluoroscopic observations reported by Webb, Forster and Gilbert¹⁷

15 Manges, W. F. *Am J Roentgenol* **11** 517 (June) 1924

16 Hearn, W. P., and Clerf, L. H. *Ann Surg* **85** 54 (Jan) 1927

17 Webb, G. B., Forster, A. M., and Gilbert, G. B. *Postural Rest for Pulmonary Tuberculosis*, *J A M A* **76** 846 (March) 1921

INCIDENCE

Partial or massive pulmonary atelectasis is encountered after all kinds of abdominal operations and after all types of anesthesia. We have observed cases develop after spinal local infiltration and regional block anesthesia nitrous oxide and oxygen and also after general anesthesia administered by either the open or the closed method with and without gas induction.

Pasternak has reported cases associated with diphtheritic paralysis of the diaphragm.

Bradford has reported massive atelectasis after gun-shot wounds of the chest abdomen thigh and buttocks and following fractures of the pelvis and femur and also has mentioned two cases in which atelectasis occurred as a sequel to ordinary pneumonia without fibrosis of the lung or thickening of the pleura.

Other authors have noticed this condition following infectious diseases in persons of various ages. In our series the youngest was a boy aged 12 and the oldest a man aged 68.

Thirty of the fifty patients were males. The greater number of females operated on makes the actual incidence 3:1. In a three year period in which there were 419 major cases in which operations had been done, thirty-two patients developed atelectasis. This constitutes at least 70 per cent of all postoperative pulmonary complications occurring within this period.

CLINICAL FORMS

From a consideration of the clinical manifestations presented in our cases, we have been able to recognize four types (1) The fulminant or frank type, (2) the moderate type, (3) the latent or mild type and (4) the transient or evanescent type

1 *Fulminant Type*—The fulminant type is the most readily recognized, presenting a unique symptom complex. It represents those cases referred to by several authors as the "collapse attack." The attack begins with a sudden sharp rise in temperature, pulse and respiration, associated with a sharp pain in the chest, dyspnea and cyanosis. The patient appears moribund, however, there is an absence of toxicity unless this complication is associated with some other acute infectious process. These patients have, in addition, a profuse diaphoresis, which necessitates frequent changing of gowns and bed clothes, coupled with pronounced facial erythema, which assumes a brick-red discoloration as described by Soltau.¹⁸ The alarming symptoms usually abate within thirty-six hours, and the further course is identical with that of atelectasis of moderate severity.

A characteristic posture, which is almost diagnostic, is assumed in this stage. The dorsal spine is bent and the head is inclined toward the affected side. The patient lies on the side involved.

Physical Examination—The postoperative examination of patients is carried out under unfavorable conditions, because the patient cannot be moved about, nor can he be made to assume a position favorable for the elicitation of certain signs.

Inspection, which should be carried out with the patient as straight as possible in bed and lying flat on his back, reveals the marked asymmetry of the chest. The affected side appears smaller, as if flattened, the interspaces are diminished in size, the ribs seem to converge, and a marked respiratory lag is present. This is in marked contrast to the apparent bulging and the exaggerated excursion of the sound side. This has been ascribed by Osler¹⁹ to a condition of vicarious emphysema developing on the unaffected side. The costal margin flares better on the affected side when the lower lobe is the seat of the disorder. This is due to the absence of the antagonistic action of the diaphragm, as described by Hoover.²⁰

There is tracheal displacement toward the affected side, most marked in atelectasis of the right upper lobe.

18 Soltau, A. B. *Brit M J* 1 544 (March) 1925

19 Osler, W., and McCrac, T. *Principles and Practice of Medicine*, New York, D. Appleton & Co., 1923, p. 639

20 Hoover, C. F. *Am J M Sc* 159 633 (May) 1920

Heart The cardiac impulse is displaced toward the affected side. The superficial area of cardiac dulness may be obscured by the normal expansion of the unaffected lung. When the entire lung or one of the upper lobes is atelectatic the displacement of the cardiac impulse is obliquely upward, toward the affected side. The cardiac displacement is most marked in cases of right-sided atelectasis.

Lungs The atelectasis may involve a part or a lobe, an entire lobe or a whole lung. Bilateral involvement may be present and thus render the diagnosis almost impossible because of a lack of appreciable alteration in the negative pressures of the two pleural cavities. When this occurs, the displacement of the mediastinal structures is slight and the physical signs dependent on the displacement are obscure. The most common site is the right lower lobe or the posterior portion of it. The area of atelectasis is triangular with the base directed toward the back. It is interesting to note that this area of the lung is commonly involved in the atelectasis of premature or weak infants as described by Holt and Howland.²¹

Dulness, flatness or impaired resonance is present over the area of

case was one of general peritonitis. In this connection, it must be remembered that the cases associated with other acute conditions doubtless show a high temperature as a result of the primary pathologic involvement, and the patients suffer an added rise in temperature because of the superimposed burden of atelectasis. In uncomplicated cases, in which simple or interval appendectomies have been performed, with the subsequent development of atelectasis, the temperature ranges between 101 and 103 F, the pulse between 110 and 120, and the respirations between 28 and 35.

A probable explanation of the hyperthermia may be found in the disturbance of equilibrium between the production of heat and the loss of heat. The skin is able to dispose of heat by conduction and radiation and by the evaporation of sweat, depending on the rate of the cutaneous circulation. Through the lung, heat is lost mainly in the vaporization of the water contained in the expired air (MacLeod¹⁴).

With the patient at rest in bed and covered with blankets, the efficiency of the cutaneous thermal regulating mechanism is decreased, hence, the burden of heat dissipation is thrown on the lungs. Normally, this transfer of function is assumed readily and is adequate, however, in the presence of pulmonary atelectasis, the alveolar surface is diminished and the organism attempts to compensate by increasing the cutaneous circulation, it is unable, however, to effect an equilibrium between production of heat and loss of heat, without a rise in temperature, even in the presence of a compensatory tachypnea.

The pulse rate is increased in proportion to the elevation of temperature, although it has been ascribed to the stimulation of the autonomic nerves and ganglia incident on the displacement of the mediastinal structures. The distress and perturbation of the patient also have been attributed by some to this cause.

The white blood count is not much influenced, it ranges from 8,000 to 12,000 in uncomplicated cases, occasionally it rises to 20,000 in the presence of other associated disorders.

2 Moderate Type—In the moderate type of atelectasis, the symptoms and signs are less severe, and the amount of pulmonary atelectasis is less extensive.

3 Latent Type—The latent cases manifest few symptoms referable to the respiratory tract and are discovered by careful observation and attention to the physical manifestations. These patients usually exhibit a considerable degree of dyspnea when placed on their unaffected side but not as marked as those with a "frank" or "moderate" type of atelectasis. The physical signs usually clear up in a few days leaving no residuum, hence, the condition is frequently overlooked. If all patients with slight fever were examined postoperatively as a routine we believe that more latent cases would be discovered.

4 *Evanescent Type*—The transient type usually presents moderate or mild symptoms, and its onset is ushered in by a sudden elevation in the temperature, pulse and respiration. The gravity of the symptoms and their duration are subject to marked variation, however the clinical picture is commensurate with the rise in the temperature, pulse and respiration, in the absence of other complicating pathologic conditions. Simultaneously with the sudden sharp rise of temperature, the patient is extremely perturbed and is apparently the subject of some catastrophe. The symptoms are those presented in a moderate type of atelectasis, and the dyspnea may be extreme. The termination is as abrupt as the onset, after several hours all the urgent symptoms disappear and the patient is apparently normal. The physical signs disappear coincidently with the clinical improvement. The abatement of the distress is almost invariably associated with the expectoration of thick, tenacious mucus.

Roentgenologic studies in these cases are meager since roentgenograms could not be secured at the proper time.

a bronchopneumonia superimposed on the atelectasis develops. Such patients exhibit an increase in the severity of the symptoms associated with a bloody expectoration and râles over the affected area. These patients, in contrast with those affected merely with an atelectasis, are definitely toxic.

Friction sounds, both pleural and cardiac, have been found in our cases, and have also been reported by others. We believe that in the great majority of the cases, in the absence of pneumonia or bronchopneumonia, the friction sound is caused by the displacement of the thoracic structures and is mechanical rather than pathologic, because it disappears with the return of the structures to their normal position.

Occasionally pleuritis, with or without effusion, may develop as a late complication.

DIFFERENTIAL DIAGNOSIS

The diagnosis of this condition is relatively easy when the clinical picture is borne in mind. Other conditions and postoperative pulmonary complications, from which differentiation must be made, include the following: pulmonary embolism or infarction, acute dilatation of the heart, pleurisy with or without effusion, subphrenic abscess, pneumothorax and diaphragmatic hernia.

Atelectasis is the only condition giving rise to a paradoxical phenomenon. The signs of consolidation of the lung are present, with a suppression of breath sounds and fremitus with retracted, immobile chest, associated with a displacement of the heart and mediastinal structures toward the affected side. In cases in which no complications have occurred, there is an absence of toxicity, and the general symptoms are not so pronounced as in the graver forms of pulmonary complications, such as embolism, infarction or pneumonia. Roentgen-ray examination at the proper time confirms the diagnosis.

Roentgenologic Examination—The roentgen-ray evidence in pulmonary atelectasis is characteristic and, if obtained at the proper time, will establish the diagnosis. The site of the atelectasis is determined, and the degree of physical displacement and distortion is demonstrated.

In order to cause the least disturbance to the patient, the examination is made with a portable machine. The patient remains in bed, and the roentgenogram is made in the anteroposterior position. The roentgenogram must be examined with special reference to the following points: the line of the vertebrae, convergence of the ribs, position of the heart, aorta and trachea, relative position of the right and left sides of the diaphragm, the presence of increased density in the affected lung and of decreased density in the unaffected lung.

In a typical case of unilateral atelectasis, the following evidence is present:

Vertebrae The dorsal vertebrae are curved laterally with the concavity toward the affected side.

Ribs The ribs converge on the affected side, and diverge on the opposite side, so that one side of the chest space is smaller than normal and the other is larger than normal.

Mediastinum The heart and mediastinal structures are displaced toward the atelectatic lung. The trachea is displaced less in atelectasis of the left side than in involvement of the right side. The most marked deviation in the trachea occurs with atelectasis of the upper right lobe.

Diaphragm The diaphragm on the affected side is elevated above its normal relative position and the opposite side of the diaphragm is lower than its normal relative position. In those cases in which the diaphragm has been markedly elevated, fluoroscopic observation shows that slight excursion is present but so slight that the diaphragm does not play any real part in the respiratory function.

Lungs On the side of the atelectasis there is increased density, localized or general. This may vary in degree from a slight increase which is barely perceptible, to a marked increase, great enough to obliterate all markings in the lung and chest. Associated with this a varying degree of decreased density is found in the opposite lung the result of the compensatory emphysema.

In bilateral atelectasis, the right and left space in the chest is small. Both sides of the diaphragm are high, but maintain their relative position, and there is no curvature of the spine. There is usually some displacement of the heart toward the more affected side.

There are many cases in which there is no gross density in the affected lung. In the moderate and mild types there may be present only an inequality of density in the two lungs, increased on the affected side and decreased on the unaffected side, associated with one or several of the following signs: displacement of the heart and mediastinal structures, elevation of the diaphragm or curvature of the spine, and convergence of the ribs.

Serial roentgenograms are useful in the study of the progress of the condition. As the patient improves the spine straightens, the ribs assume their normal appearance, the heart and mediastinal structures, and the diaphragm gradually return to their normal position, and densities in the lungs equalize.

It cannot be too strongly emphasized that mild cases of atelectasis only when gross density in the lung is present will go unrecognized.

The roentgen-ray signs cannot be overlooked in the absence of clinical evidence, nor can the severity of the condition be judged by the roentgen-ray evidence. In many cases the clinical symptoms are the only evidence of the condition.

PATHOLOGY

In two cases at autopsy, Jackson and Lee¹ have been able to demonstrate plugs of mucus sufficient to cause complete obstruction to the bronchial lumen and, *in vivo*, have observed obstructing masses of mucus by means of the bronchoscope. Further bronchoscopic observations by Lee and Tucker¹⁰ have shown an injection of the bronchi as an indication of a mild catarrhal inflammation.

When the chest is opened at autopsy, the lungs do not fill the pleural cavities, and a peculiar swishing sound is produced by the air entering the chest, followed by a return of the retracted wall to its normal position.

Ritvo²³ gives an adequate description of the lung obtained at post-mortem. "The involved portion of the lung is blue or violet in color and sharply demarcated from the normal lung tissue. It is soft, tough and wet, it feels heavy, does not crepitate, and sinks when placed in water. Microscopically, the alveolar surfaces are closely approximated, the alveolar spaces being obliterated." These observations were confirmed at necropsy in one of our cases.

In uncomplicated atelectasis, cellular infiltration is absent, indicating the nonexistence of inflammatory reaction.

TREATMENT

Many observers attempted the amelioration of this condition by the administration of various drugs, especially those producing an effect on the autonomic system, but apparently without benefit. The treatment has therefore been relegated to the symptomatic group unless a complicating condition arises, in which case the treatment is that of the complication.

Elliott and Dingley⁴ advised "keeping the lung open," by encouraging the patients to inspire deeply for five minutes every hour during the first few days after operation, and admonished against the use of tight bandages and straps which restrict the free respiratory act, on the ground that such restriction favors the onset of atelectasis. These authors have employed expectorants and potassium iodide with apparent success. They recommend the production of an artificial pneumothorax on the affected side to relieve the cardiac embarrassment although they have not used it. Farris²⁴ has employed this method with apparent benefit in one instance and urges its use in established cases.

An important contribution to the realm of therapy was the institution of bronchoscopic examination coupled with the aspiration of the

23 Ritvo M. *Am J Roentgenol* 11 337 (April) 1924

24 Farris H. A. *Canad M A J* 15 808 1925

right, she continued about the same during the night. In the early morning, the nurse reported that she complained of pain on inspiration. The temperature dropped to 101.2, the pulse was 110, and the respirations 28, at noon on December 30. That afternoon the temperature again rose to 104.6. The pulse was 138, the respirations 40, and marked friction rub was present at the base, the breath sounds were absent and the trachea deviated to the right. The condition continued about the same over night, in the early morning a productive cough began, and the patient spat up a large amount of greenish mucopurulent secretion, which relieved her considerably.

The temperature dropped to 100, the pulse to 100, and the respirations to 26 on December 31, the symptoms gradually cleared.

Roentgen-ray examination confirmed the diagnosis.

CASE 2—A white man, aged 22, unmarried, was admitted to the hospital, Nov. 27, 1926. The condition was diagnosed as acute appendicitis. The patient was operated on at 2 p. m., and a ruptured retrocecal appendix was found and removed. The temperature was 101, pulse 100, and respirations 20 at the time of the operation. The patient was placed on Clark's peritonitis treatment immediately. The reaction from the operation brought the temperature up to 101.2, the pulse to 110 and the respirations to 24 at midnight. The following day, he appeared fairly comfortable until the late afternoon, when he complained of increasing dyspnea, profuse diaphoresis and hacking, nonproductive cough. Marked brick red, dusky cyanosis was present. Physical examination at 8.30 p. m. disclosed a marked limitation of movement on the right side, dulness to percussion in the lower right lung and distant breath sounds over this area—apex beat about 3 cm. to left of sternal line. The trachea was displaced to the right. At 4 a. m., on November 28, the temperature was 104.8, pulse, 126, and respirations, 44. During the early morning, he began having a productive cough and brought up large quantities of mucopurulent secretion, after which he felt somewhat relieved. The temperature had dropped rapidly to 100.8, the pulse to 88, and the respirations to 30 at noon on November 29. The symptoms then gradually subsided, and on December 1, no signs were present in the chest.

CASE 3—A white girl, aged 17, single, was admitted to the hospital, Aug. 18, 1926. The diagnosis was acute suppurative appendicitis, and operation was performed at 6 p. m. under gas induction followed by ether vapor and oxygen the anesthesia lasted thirty minutes. The abdomen contained free fluid, drainage was instituted and the patient was placed on Clark's peritonitis treatment immediately. The temperature was 102.8, the pulse 135 and respirations 28 at the time of the operation. The temperature was 104.2, the pulse 140, and respirations 22 at midnight on the day of operation. The next day the temperature was 102.4, pulse, 130, and respirations, 24, the patient apparently was doing well. On the 19th she complained of much mucus in the throat and coughed up considerable thick tenacious material. That night the nurse turned her on her left side and stepped out for water, she stated that she was not gone more than five or ten minutes. When she returned she found the patient cyanotic, dyspneic and sweating profusely and apparently moribund. The temperature was 105.4, the pulse 154, and respirations, 54, physical examination was limited to the right side of the chest, the upper right side was literally drowned with coarse, bubbling râles. The breath sounds were absent in the lower right base with dulness to percussion. The apex beat was about 2 cm. from the left sternal border. The trachea was markedly displaced to the right. This condition continued during the night, but the patient felt somewhat improved by noon on August 20. When it was attempted to make the patient comfortable and she was turned on

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On February 14, the condition of the chest changed, and it presented the typical signs of bronchopneumonia—almost flatness on percussion, marked impairment of the right side of the chest, increased breath sounds, whispered pectoriloquy and bronchial râles throughout the right side of the chest, but with the displacement of the heart and the mediastinal structures to the right. The patient gradually improved, though with several relapses of cyanosis, dyspnea, etc.

On February 16, he suddenly coughed up a great deal of thick, mucopurulent material and felt much relieved. The final roentgenogram showed evidence of pathologic changes remaining in the lung.

On February 10, the white blood cells numbered 14,600, and on February 20 they numbered 8,900.

On the 18th, the vital capacity of the lungs was —700 cc, and on the 20th, it was —800 cc.

CASE 6—A white man, aged 44, was admitted to the hospital, Jan 23, 1927. The diagnosis was recurrent right inguinal hernia. The patient was operated on the following day under nitrous oxide induction and ether, he was under the anesthesia one hour and forty minutes. He coughed considerably shortly after he recovered from the anesthetic, it was thought that this man was the type to develop an atelectasis, and therefore he was carefully watched.

The temperature was 99, pulse, 82, and respirations, 18 on the day of the operation, the operative reaction brought the temperature to 100.6, the pulse to 96, and the respirations to 22.

On January 26, the temperature was 102.4, pulse, 130, and respirations, 36, these gradually ascended till on January 27, the temperature was 103.8, pulse, 132, and respirations, 40.

On January 26, physical examination showed marked cyanosis of the lips and nails, brick red erythema of the face and neck and marked diaphoresis and dyspnea. The right side of the chest showed marked limitation of motion, and even the intercostal spaces could be made out much narrower on the right side, the patient's position also was characteristic, the head was drawn to the right and the thorax inclined to the right. The heart and mediastinal structures were also drawn to the right, dulness was present over the right upper and middle lobe, breath sounds were distant, with absent vocal fremitus and tactile fremitus.

Pleuritic friction rub was present over the upper part of the sternum on the right side, at this time the cough was practically nonproductive and was irritating. The patient complained constantly of "mucus in the throat" that could not be raised.

On January 27, the physical examination was essentially the same, except that coarse râles were now heard, and that the cough was more productive. The patient expectorated large amounts of thick, tenacious mucopurulent material.

On January 30 there were still evidences of pathologic changes in the right lung.

On February 1, the lung was found to be clear, and the roentgenograms were negative (fig 1).

CASE 7—A white woman, aged 47, was admitted to the hospital, March 3, 1927. The diagnosis was chronic cholecystitis and cholelithiasis. The patient was operated on the following day under gas (N₂O) and ether anesthesia. The operation lasted two hours as considerable difficulty was encountered in removing the gallbladder. The temperature was 98.8, pulse 86, and respirations 20 at the time of the operation. The following morning the temperature was 104.2, pulse 126 and respirations 30.

At noon, on March 4, she began perspiring profusely, was deeply cyanotic and erythematous and was lying with the head toward the right side the temperature had dropped to 100.6 at noon, but that night it was 104 pulse 142 and respirations, 36, and the patient appeared moribund.

She began coughing and soon brought up large quantities of thick tenacious, mucopurulent material.

The condition cleared up gradually, and on March 8 the chest was reported clear.

The condition was confined to the right lower lung, the patient was obese, and physical signs were far from accurate, suppression of the breath sound, dullness over this area and slight deviation of the trachea to the right were present.

CASE 8—A white boy, aged 16, was admitted to the hospital, Feb. 12, 1927. The diagnosis was acute appendicitis. Operation was performed the same day,



Fig. 1 (case 6) — Appearance of lungs Jan. 26, 1927 showing involvement of the right upper lobe and marked displacement of the trachea and the mediastinal structures.

under gas (N₂O) and ether anesthesia and listed twenty-five minutes. The abdomen contained pus and the appendix was ruptured. The temperature 102.4 pulse 104 and respirations 34 at the time of operation. The patient placed on Clark's peritonitis treatment immediately.

That night the temperature was 105.2 and dropped to 102.2 the next day but the following day the patient became cyanotic and dyspneic perspired profusely and seemed moribund. The temperature was 106.0 pulse 142 and respirations 46 the temperature the next day had dropped to 102.2 and continued a downward course.

The physical symptoms were definite and typical of pulmonary consolidation. The right side of the chest was dull with decreased breath sounds and hyperresonance on the left. Displacement of the heart and mediastinal structures to the left.

chest showed marked retraction of the intercostal spaces and marked limitation of movement. The lower costal margin moved outward from the midline farther than on the left.

The patient continued to be extremely ill for several days, but about the twelfth or fourteenth day the chest was normal. The roentgenograms were negative.

CASE 9—A white man, aged 32, was admitted to the hospital, Feb 22, 1927. The diagnosis was ruptured duodenal ulcer. Operation was immediately performed, and a gangrenous, ruptured appendix was found. The patient was at once placed on Clark's peritonitis treatment. The temperature was 100.6, pulse, 100, and respirations, 20 at the time of operation, that night it receded somewhat. The patient's condition seemed fairly good.

On February 24, the temperature was 104.4, pulse, 144, and respirations, 24. The respiration remained low because of the morphine he was receiving, he became markedly cyanotic and dyspneic and sweated profusely, the pathologic change was limited to the right middle and base of the lung. Distant breath sound was present. Vocal and tactile fremitus were absent.

On February 25, the temperature was 100, pulse, 86, and respirations, 20, and symptoms in the chest were scant.

On February 26, the chest was normal.

CASE 10—A white man, aged 41, was admitted to the hospital Feb 22, 1927. The diagnosis was subacute appendicitis, and operation was performed the same day under local field block and light gas (N₂O) and oxygen. The anesthesia lasted for about one hour, from twelve to eighteen hours after the operation he complained of shortness of breath and a tightness through the right side of the chest. The next day he was perspiring profusely, was markedly cyanotic and erythematous, and appeared moribund. The temperature was 100, pulse, 100, and respirations, 22 at the time of the operation, the next day, the temperature was 106, pulse, 146, and respirations, 40. The temperature remained high for two days.

On February 25, the temperature was 100.4, the pulse, 80, and respirations, 20. The entire right side of the chest was practically immobile and the intercostal spaces narrowed. The patient was lying on the right side with the head drawn well over, and the heart and mediastinal structures markedly displaced to the right. He began coughing on February 24, and spit up great quantities of thick tenacious material, the chest showed many coarse rhonchi at this time, and dullness was less marked.

On February 28, the chest was reported clear. The roentgenogram was positive (figs 2, 3 and 4).

CASE 11—A white woman aged 55 was admitted to the hospital, Jan 7, 1927. Obstipation was present for five days. A palpable mass was present in the upper right quadrant and also a patch of bronchopneumonia in the left base, the patient was extremely ill. Operation was performed early the next day under local block, with 1 per cent procaine hydrochloride. A gangrenous gallbladder was found with marked adhesions in the hepatic flexure giving symptoms of obstruction. Many stones were found in the gallbladder.

The temperature was 99.2, pulse, 100, and respirations, 20 at the time of operation. Late that day the temperature was 103, pulse, 138 and respiration, 24. The patient was gradually growing weaker, but not until January 9 did her condition suddenly become grave. About 5 p. m. she suddenly became cyanotic and dyspneic and the pulse very rapid. Profuse diaphoresis was present, the temperature was 105.2, pulse 144, respiration 38. There was more definite evidence of pneumonia on the left side but not as great involvement as would



Fig 2 (case 10) —Appearance, Feb 23, 1927, showing complete signs of typical atelectasis on the right side and compensatory emphysema on the left side.

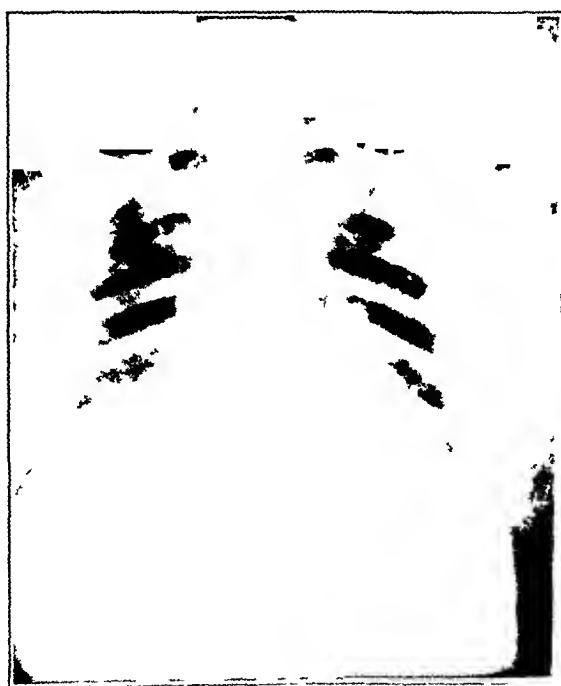


Fig 3 (case 10) —Appearance of lungs on March 14, 1927, showing increased density at the right base. The other signs are absent.

be expected with so sudden a change for the worse, a roentgenogram was made with a portable roentgen-ray apparatus and showed that the right upper lobe was collapsed, with marked deviation of the upper portion of the trachea to the right, she also began coughing and expectorated considerable mucopurulent tenacious material, the temperature was 102, pulse, 120, and respiration, 24 the next morning

She gradually became weaker and died from toxemia at 9 45 p m, Jan 10 1927 Autopsy was refused

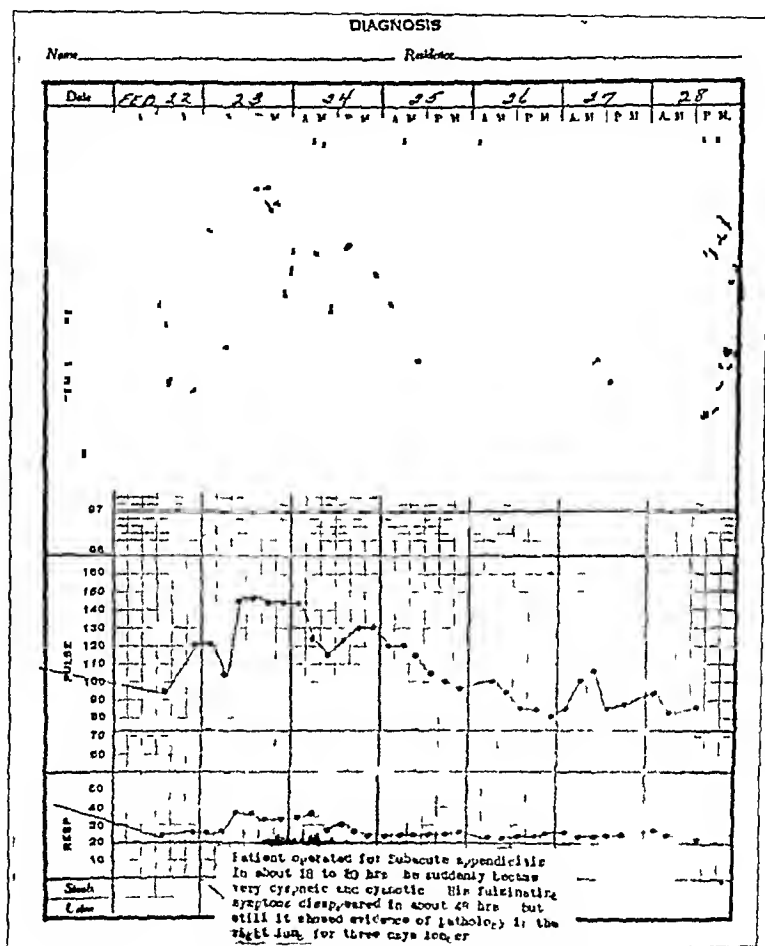


Fig 4 (case 10) —Summary of course of atelectasis

CASE 12—A white woman, aged 42, was admitted to the hospital, May 2 1926. The diagnosis was subacute cholecystitis. The operation, consisting of cholecystectomy and appendectomy, was performed the following day under drop ether, the anesthesia lasted for one hour and ten minutes. The temperature was 99, pulse 82 and respirations, 20 at the time of operation. The next day the patient's condition was reported as good. The following morning she complained of pain in the left side of the chest and marked dyspnea. She became cyanotic, and marked diaphoresis was present. At the same time a distressing cough began. At 4 p m the temperature was 103, pulse, 132, and respirations, 44. Dulness over the left lower lung base, a distant breath sound and displacement of the mediastinal structures to the left were present. In about twelve or

fifteen hours, she began expectorating large quantities of a thick tenacious mucopurulent material. The abdomen became greatly distended and there was a profuse drainage of bile from the incision. She failed rapidly and died May 7 of probable peritonitis, acute dilatation of the stomach and myocardial failure. Autopsy was refused. The roentgenogram confirmed the diagnosis of left-sided atelectasis (fig 5).

CASE 13—A colored man, aged 28, was admitted to the hospital Feb 19 1926. The diagnosis was made of right lobar pneumonia. The temperature was 104.2, pulse, 120, and respirations, 32, the pneumonia ran an unusual course which was probably due to the fact that the patient had been given a course of ethylhydrocuprein hydrochloride.

The temperature dropped to normal and remained there for a period of about five or six days, and the patient was convalescing rapidly.



Fig 5 (case 12)—Appearance of lungs on Jan 10 1927 showing atelectasis of the upper right lobe, marked displacement of trachea to the right, pneumonia consolidation in the left lung, marked density in upper right lobe and compensatory density in the middle and lower right lobe due to compensatory emphysema.

Suddenly, early one morning he became greatly distressed and was unable to breathe. He perspired profusely and began coughing. On examination the right side of the chest was dull to percussion but breath sounds were present. The heart was pulled to the right. The patient was thought to have a right-sided empyema or pleurisy with effusion but cardiac displacement was not confirmed. A roentgenogram was then made which showed a large consolidation in the right lung.

The condition cleared up in about ten days and the patient was well recovered but three days later he again was troubled with the same complex. The second time required less treatment.

The patient left the hospital Feb 25 1927. He was well and had no right base.

This case was not a postoperative one, but is interesting because of its apparent rarity as a complication of pneumonia

This condition may also be the answer to why many so-called relapses clear up rapidly

Cases 11 and 12 were really complicated by other conditions which aided in the production of marked elevation of temperature

The next group of seventeen cases are of the moderate type

MODERATE TYPE

CASE 14—A white woman, aged 30, was admitted to the hospital, Jan 25, 1927. The condition was diagnosed as chronic cholecystitis, cholecystotomy was carried out under gas (N₂O) and ether anesthesia on January 26, the anesthesia lasted forty minutes. The patient recovered from the anesthetic poorly and complained of much mucus in the throat. The temperature was 98.4, pulse, 90, and respirations, 20, at the time of the operation, during the next twenty-eight hours, she complained of tightness in the chest, she sweated profusely and the face was suffused with a dark red blush and some cyanosis of the lips and nails. The temperature was 102.2, pulse, 136, and respiration, 36, on January 28, she began expectorating moderate quantities of tenacious mucopurulent material on the second day. The condition cleared gradually, the chest was clear at the end of five days. The roentgenogram was positive.

CASE 15—A white woman, aged 25, was admitted to the hospital, Jan 3, 1927. The diagnosis was retroversion and erosion of the cervix. The patient was operated on the following day under gas (N₂O) and ether anesthesia, the duration of the anesthesia was one hour. At the time of the operation, the temperature was 98.2, pulse, 86, and respiration, 18. The condition was good till about twenty-four hours later, when she began complaining of mucus in the throat and an annoying, nonproductive cough. Coincidentally with this she began perspiring profusely and was definitely cyanotic and dyspneic with a marked brick red discoloration of the face and neck. The temperature was 102.6, the pulse, 140, and respiration, 54, dulness was present over the right side of the chest, and there was a distant breath sound in the right base. Coarse rales were present above the dull area, there was limitation of the chest movement on the right side.

On January 5, she began expectorating large amounts of thick, tenacious, mucopurulent material, after which she was considerably relieved.

The condition apparently cleared up, but the patient again developed a cough, which lasted in all about eight days. We thought that she had a purulent bronchitis superimposed on the already existing atelectasis.

CASE 16—A white man, aged 21, was admitted to the hospital Jan 14, 1927. The diagnosis was left inguinal hernia, operation was performed the following day under gas (N₂O) and ether. The duration of the anesthesia was thirty minutes, at the time of the operation, the temperature was 98.4, pulse, 80 and respirations 20. This patient was annoyed early in the course of the illness by hacking nonproductive cough and much mucus in the throat.

The following day, in the late afternoon, he complained of pain in the chest, and dyspnea, which are characteristic of this condition. Cyanosis of the lips and nails, brick red erythema of the face and neck, profuse diaphoresis, limitation of motion in the left side of the chest and distant breath sound in the left lower half of the chest were present. The temperature was 102.2, pulse, 112, and respiration 30. Here again the graphic chart belies the apparent clinical

severity. He began expectorating large quantities of thick tenacious yellow material and improved rapidly, the chest was clear January 19. The roentgenograms were positive.

CASE 17—A white man, aged 39, was admitted to the hospital Dec. 20, 1926. The condition was diagnosed as chronic cholecystitis and appendicitis.

He was not operated on until December 31 when an appendectomy and cholecystectomy were done. The temperature was 98.4, pulse 82 and respiration 20, at the time of operation. The operation was done under gas (N₂O) and ether, lasting one hour and twenty-five minutes, this patient also complained of troublesome mucus in the throat, soon after recovery from the anesthesia. He also complained of cough and pain in the chest.

Twenty hours after the operation, the temperature was 103.4, pulse 134 and respirations 38. The patient was perspiring profusely, marked cyanosis of the lips and nails, and the peculiar brick red erythema also were present.

He began expectorating the thick mucopurulent material rather early, twenty-four hours after the operation and continued for several days. On physical examination, the right side of the chest was found to be limited in movement, dull in the lower right lobe, with distant breath sound and apex beat pulled to the right.

Roentgen-ray examination showed the diaphragm to be high on the right.

The condition gradually cleared up but the patient left the hospital with slight pathologic changes in the right base.

CASE 18—A white woman, aged 44, was admitted to the hospital Feb. 14, 1927. The diagnosis was subacute cholecystitis and cholelithiasis. Operation was performed, February 15, under gas (N₂O) and ether anesthesia, the duration of the anesthesia was forty-five minutes, the patient did badly under the anesthesia and alpha lobeline, $\frac{1}{4}$ grain (0.01 Gm.), was given on the table to stimulate respiration. At the time of the operation, the temperature was 97.6, pulse 80 and respirations, 20.

That same evening she began having profuse diaphoresis and was considerably disturbed by hiccoughs, this lasted for about ten hours. The next morning she began coughing nonproductively at first but later she began expectorating a moderate amount of thick tenacious mucopurulent material.

On February 16, the temperature was 103.4, pulse 134 and respiration 20.

The same morning she was cyanotic and dyspneic, the reddish cyanosis blended with the preexisting icterus, this produced a peculiar grayish color and the patient appeared moribund.

She expectorated considerable thick tenacious material and when relieved, the condition did not entirely disappear nor did the hiccoughs.

This patient also had a substernal thyroid which made the examination of dullness in the right side of the chest, absent breath sound, and displacement of the trachea to the right somewhat doubtful. However, repeated roentgen examinations made the complications clear.

CASE 19—The patient was admitted to the hospital September 19, 1927. The diagnosis was congenital bilateral indirect hernia. On admission the patient had emphysema and a large hernia on the right side. On the 14th when a bilateral hernia repair was performed. At the time of the operation the temperature was 98.6, pulse 120 and respirations 20. The operation performed lasted one hour and fifteen minutes. The patient was cyanotic and dyspneic, the temperature was 100.2, pulse 140 and respirations 30. The operation was done well but the patient was very weak and the condition was not improved.



Fig 6 (case 19) —Appearance of lungs on Sept 18, 1926, showing atelectasis of the left lung, marked displacement of the heart and aorta to the left, high left side of diaphragm, marked density in the left lung and decreased density in the right lung



Fig 7 (case 19) —Normal appearance of lungs on Feb 23, 1927

to be improved, but still coughed at infrequent intervals and raised a small amount of yellowish purulent material about 8 p. m.

On September 15, he complained of pain in the left side of the chest and difficulty in breathing, he was perspiring profusely and the nurse reported him as being very "redfaced." Examination revealed the left side of the chest greatly limited in expansion, dullness in the base of the left lung, with distant breath sound, and almost absent tactile and vocal fremitus. The trachea was somewhat displaced and the apex was in the axillary line. This condition continued through the 16th, and on the 17th he was greatly improved clinically but still showed

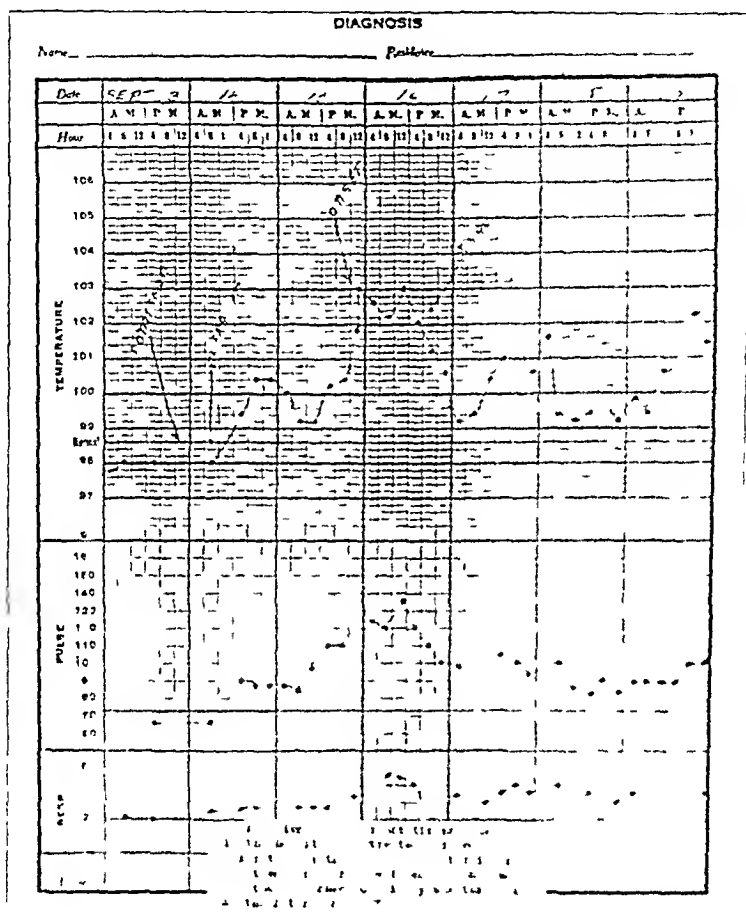


Fig. 8 (case 10)—Summary of course of infection.

physical signs. On the 16th he had another severe attack, but it cleared up in about twenty-four hours.

On the 22d he had entirely returned to normal condition.

Röntgen-ray examination was carried out on September 22.

CASE 20—A white girl, aged 12, was admitted to the hospital on September 10. The diagnosis was subacute type of tuberculosis. On the morning under drop ether anesthesia, which was given, the temperature was 99.2, pulse 110, respiration 22. On the 11th the temperature was 99.2, pulse 110, respiration 22. On the 12th the temperature was 99.2, pulse 110, respiration 22. On the 13th the temperature was 99.2, pulse 110, respiration 22. On the 14th the temperature was 99.2, pulse 110, respiration 22. On the 15th the temperature was 99.2, pulse 110, respiration 22. On the 16th the temperature was 99.2, pulse 110, respiration 22. On the 17th the temperature was 99.2, pulse 110, respiration 22. On the 18th the temperature was 99.2, pulse 110, respiration 22. On the 19th the temperature was 99.2, pulse 110, respiration 22. On the 20th the temperature was 99.2, pulse 110, respiration 22. On the 21st the temperature was 99.2, pulse 110, respiration 22. On the 22nd the temperature was 99.2, pulse 110, respiration 22.

cyanotic, profuse sweating and a hacking, nonproductive cough were present. The temperature was 102.8, pulse, 150, and respirations, 32.

Examination revealed limitation of movement of the left side of the chest, impaired resonance over the left lower lobe, suppressed breath sounds, and apex beat in the axillary line, with very little, if any, displacement of the trachea. The peculiarity of these symptoms was that nearly all of the symptoms in the chest were elicited posteriorly, and very few, if any, could be elicited anteriorly; this is explained by figure 9, which showed the left side of the diaphragm to be higher, the heart and mediastinal structures to the left, and the lung clear, the shadow of the heart was over to the axilla, thus obliterating the patch of atelectasis that must have been behind the heart shadow.

The clinical symptoms had practically disappeared by January 21, but the heart was still displaced, and the diaphragm up when the patient was discharged. She

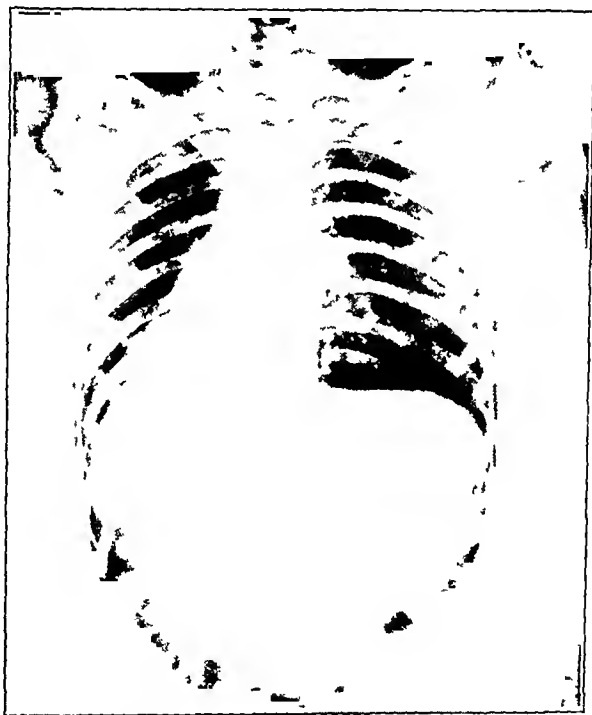


Fig 9 (case 20) —Appearance of lungs on Jan 21, 1927, showing atelectasis of the left lung, displacement of the mediastinal structures to the left, lateral curvature of the spine, with concavity toward the left. The atelectatic area is behind the heart density in the left lung. Increased density in the right lung.

spit up considerable yellow mucopurulent material, which greatly relieved the symptoms.

CASE 21 —A white boy, aged 18, was admitted to the hospital, March 17, 1926. The diagnosis of subacute appendicitis was made, and operation was performed the next day under gas (N₂O) induction and ether, the anesthesia lasted for forty minutes. The abdomen was closed without drainage. The temperature before the operation was 98.4, pulse, 78 and respirations, 22. The reaction from the operation caused a temperature of 99.4, pulse, 88, and respirations, 20.

The patient apparently was doing well, when in the early morning of the 19th he began to cough occasionally. The cough was irritative and nonproductive. The temperature was 101, pulse, 92 and respirations 28. This condition continued until

the afternoon, when he became markedly cyanotic dyspneic and began perspiring profusely. The temperature at 9 p. m. was 103.6, pulse 110 and respirations 48. The patient was coughing frequently, but the cough was still nonproductive. Marked dyspnea, cyanosis and erythema of the face and lips were present. The patient was lying on the right side, dullness over the right base with diminished breath sound, were present. The trachea and mediastinal structures were displaced to the right apex 3 cm. from the left sternal border.

On March 20, the condition was essentially the same. The next day the temperature and the pulse had subsided to some extent and the patient was considerably relieved. The symptoms persisted with gradual moderation until March 26. The chest still showed some evidence of pathologic change although clinically the condition was satisfactory.

On March 24, the patient coughed up large amounts of thick tenacious mucopurulent material, after which recovery was more rapid.

CASE 22—A colored boy, aged 15, was admitted to the hospital Dec. 1, 1926. At this time a tonsillectomy was performed, and he was sent home to return later.

The second admission was on Dec. 27, 1927, under drop ether (open method) an orchidectomy on the left and a Ferguson herniotomy were performed.

At this time, we were considering vagus control in order to determine the etiology of collapse, so the left vagus was vigorously stimulated by rubber. The temperature was 97.6, pulse 68 and respirations 29 at the time of operation. At midnight, the temperature was 98.8, pulse, 100, and respirations 22.

On December 29 he began coughing slightly and complained of pain in the chest, chiefly on the right side. That afternoon he became dyspneic and perspired a great deal. He was lying in bed with the head and neck inclined to the right. The temperature was 102.8, pulse, 132 and respiration 38. The lips and finger nails were cyanotic, as the patient was colored the other erythematous phenomena could not be observed. Vocal and tactile fremitus were absent. A distant breath sound was present. The trachea and the mediastinal structures were displaced

day under gas (N_2O) and ether, the anesthesia lasted thirty minutes. In the evening, she complained of mucus in the throat but did not begin coughing until the following day. The temperature was 102.4, pulse, 124, and respirations, 34. In the late afternoon of February 25, the temperature was 97.8, pulse, 90, and respirations, 20, at the time of operation. Physical examination revealed moderate cyanosis, marked diaphoresis, dulness over the lower part of the right lung, distant breath sound and limitation of motion in the right side of the chest and questionable displacement of the apex and mediastinum. The patient coughed up

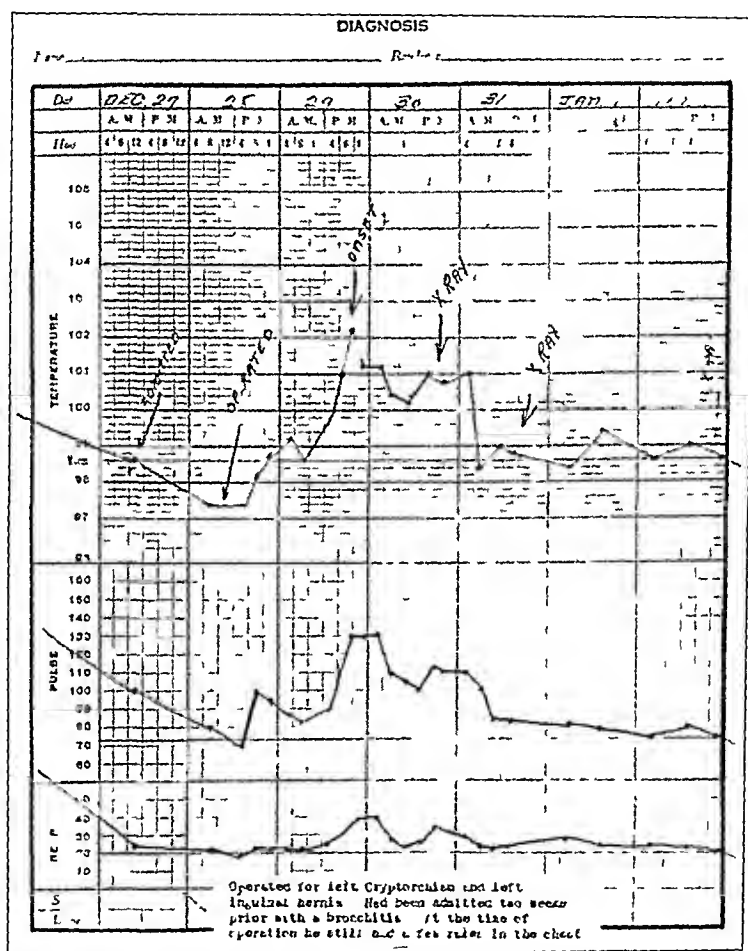


Fig 10 (case 22) —Summary of course of atelectasis

a moderate amount of thick tenacious, mucopurulent material on the 26th, and the chest was entirely clear on the 28th.

CASE 25—A white woman aged 35, was admitted to the hospital, Feb 21 1927. The diagnosis was retroversion, 3 degrees. Stenosis of the cervix and hemorrhoids were found. Operation was performed the following day under gas (N_2O) and ether. The duration of the anesthesia was one hour and five minutes. The temperature was 98, pulse 84 and respirations, 18 at the time of operation. The patient complained of considerable mucus in the throat on awakening from the anesthesia. In the early morning of the 23d, she began coughing and complained of pain in the left side of the chest, she began perspiring freely, the night nurse reported the patient as 'very red-faced and having trouble breathing.'

The upper quadrant of the left side of the chest was dull and a distant breath sound, limited movement and marked erythematous flush were present. The patient began coughing at this time. The temperature was 101.6, pulse 114 and respirations, 28. She spit up considerable mucopurulent material. This condition of the chest disappeared in about forty-eight hours.

CASE 26—A white man, aged 40, was admitted to the hospital Feb. 9, 1927. The diagnosis was bilateral indirect hernia. Operation was performed on February 11, 1 per cent procaine being used for field block. The patient had nasopharyngitis and was coughing occasionally. The temperature was 97.4, pulse, 68, and respirations, 18, at the time of operation. He continued coughing and the next day began perspiring profusely and became dyspneic. Marked erythema appeared on the face and neck. The temperature was 101.6, pulse 114 and respirations, 38. In the late afternoon of the 12th he presented the following symptoms: nonproductive coughing, a feeling of tightness in the chest and marked cyanosis and erythema when he lay on the right side. There was dullness to percussion over the right side, distant handbox sound and marked limitation of motion in the right side of the chest. The intercostal spaces were markedly retracted. He expectorated considerable purulent tenacious material but continued to present symptoms for six or seven days. The chest was reported normal on the 18th.

change was limited to the right lower lung, diminished breath sound, dullness to percussion and moderate displacement of the heart and mediastinal structures to the right were present

On February 18, the chest was reported normal, in the interim, he expectorated much tenacious, yellow mucopurulent material. Roentgen-ray examination was positive for atelectasis in the right base

CASE 29—A white boy, aged 18, was admitted to the hospital, Feb 23, 1927. The diagnosis was bilateral indirect inguinal hernias. Operation was performed the following day under spinal anesthesia, 10 cc of 1 per cent procaine hydrochloride being injected in the second lumbar interspace, this form of anesthesia was used because the patient had a bronchitis. The temperature was 97.6, pulse, 70, and respirations, 18, at the time of operation, there was no reaction from the spinal anesthesia, the patient was troubled during that night with a hacking cough, but was no worse than on admission. Early the following morning, he became definitely cyanotic and dyspneic, with marked diaphoresis. The temperature was 101.2, pulse, 110, and respirations, 36. The cough became productive, examination at this time showed some dullness over both lower lobes, but most marked over the right, distant breath sound and some limitation in movement of the wall of the chest. The heart and mediastinum were somewhat displaced to the right. The patient began spitting up large quantities of mucopurulent material, and the condition cleared up rapidly, no evidence of pathologic change being found in the chest on February 27, except a few coarse râles, which were inconstant.

CASE 30—A white man, aged 40, was admitted to the hospital Feb 1, 1927. The diagnosis was chronic duodenal ulcer. Posterior gastro-enterostomy was done, Feb 7, 1927, under gas (N_2O) and ether, the duration of the anesthesia was two hours and fifteen minutes. Considerable difficulty was experienced in mobilizing the jejunum.

At the time of the operation, the temperature was 97.6, pulse, 70, and respirations, 20. The following day, the temperature was 102.4, pulse, 106, and respirations, 28, the patient was moderately cyanotic, but was quite dyspneic, and had marked facial erythema. He appeared much sicker than the temperature chart showed.

He was lying with the head inclined to the right. Examination revealed marked limitation of motion in the right side of the chest, distant breath sound over the right base, dullness on percussion and moderate displacement of the apex to the right. The following day he began coughing and expectorating moderate amounts of thick, tenacious, yellow material, the condition in the chest improved, but rhonchi were present.

On February 11, the chest was found to be clear. The roentgenogram showed evidence of atelectasis in the right base.

MILD TYPE

CASE 31—A white woman, aged 24, was admitted to the hospital, Jan 10, 1927. The diagnosis was bilateral salpingitis. The patient was operated on the following day under gas (N_2O) and ether. The duration of the anesthesia was one hour. The same evening the temperature was 102.2, pulse, 124 and respirations, 30 in contrast with a temperature of 98.4, pulse, 90, and respirations, 20, at the time of operation. She perspired profusely and complained of mucus in the throat and marked erythema of the face. The temperature dropped suddenly the next day and was normal at 4 p m, January 12.

She spit up considerable mucopurulent tenacious material and felt much relieved. Dullness in the lower part of the right lung distant breath sound

over this area, questionable displacement of the mediastinal structures and a few coarse rales in the upper part of the right side of the chest were found. He continued to spit up a moderate amount of this material for three days. The clinical syndrome disappeared in about thirty-six hours.

CASE 32—A white man, aged 27, was admitted to the hospital Jan. 1, 1927. The diagnosis was subacute appendicitis. Operation was performed the following day. The wound was clean, so no drainage was used. The anesthetic used was gas (N_2O) and ether, and the operation lasted fifty minutes. Within an hour after the operation, he complained of cough and mucus in the throat and showed brick-red erythema of the face and neck; the next morning he was spitting up great quantities of thick, tenacious, mucopurulent material. It was thought that he had an acute abscess of the lung from the amount of the material expectorated. The temperature was 101.2 , pulse 120 and respirations 36. His distress was much more marked than was evidenced by the graphic chart.

On January 4, he was still spitting up large amounts.

On the 5th, he was comfortable, the temperature was 98.4 , pulse 92 and respirations, 20, the condition having cleared up practically over night. A roentgenogram taken late on the 4th was reported normal. In earlier pictures a mass was missed.

The condition cleared up by lysis and the chest was clear, February 6

CASE 35—A white man, aged 36, was admitted to the hospital, Jan 17, 1927. The diagnosis was subacute appendicitis. Operation was performed the following morning under gas (N_2O) and ether. The anesthesia lasted forty-five minutes. Some difficulty was experienced in removing the appendix, as it was firmly bound to the cecum by adhesions. The temperature was 98, pulse, 80, and respirations, 20, at the time of operation. The temperature reached 100 that night, the pulse, 86, and respirations, 20. Soon after the operation, the patient began hiccoughing, which persisted for about twenty-eight hours and which was finally checked by the old-fashioned expedient of holding out the tongue for five or ten minutes.

On January 19, in the morning, he began complaining of severe pain in the chest and began coughing, the cough was nonproductive, but very distressing. At this time he also became cyanotic and a brick red erythema of the face and

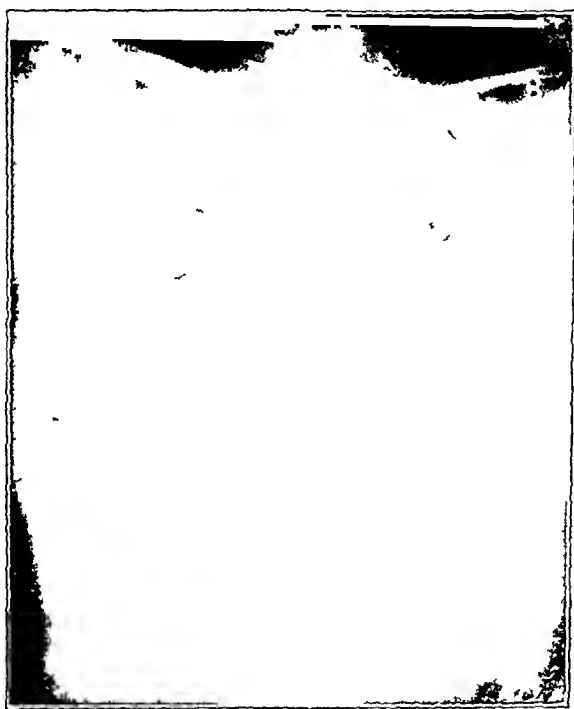


Fig 11 (case 33)—Appearance of lungs on Feb 17, 1927, showing involvement of the left lung, spine curved laterally, with concavity toward the left. The left ribs converge, and the right ribs diverge. The heart is displaced to the left. The left side of the diaphragm is elevated. Increased density in the left base.

hands appeared. The diaphoresis became so profuse that a change of bed clothing was necessitated four or five times daily. Physical examination disclosed marked displacement of the mediastinum to the right, diminished breath sound over the right lung, a few rales and marked pleuropericardial friction rub. There was a marked asymmetry between the right and left sides of the chest. Inspection showed an immobilization of the right side of the chest. A peculiar condition was found on percussion: a "strap-like" area of dulness was found extending from the fourth to the sixth interspace on the right side of the chest anteriorly, and below this a booming resonance could be heard. This was explained by the roentgenogram taken shortly after, which showed that the diaphragm had been displaced upward so far that a great dome had been formed

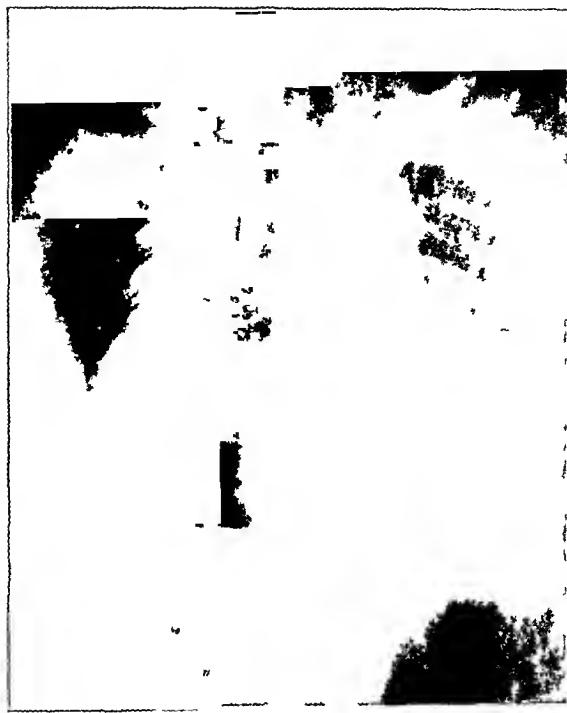


Fig 12 (case 35) — Appearance of lungs on Jan 19 1927 showing elevation of the right lung, especially at the base. The mediastinal structures are displaced to the right. Marked displacement of the right side of the diaphragm is present. The liver is displaced up with the diaphragm so that its lower border is on the same level with the left side of the diaphragm. Marked density at the base of the right lung, general increased density in the rest of the right lung, decreased density in the left lung are present.



which had pulled the liver along, thus eliminating the usual liver dulness. The condition in the chest persisted for several days and abated by lysis. The highest temperature was 101.6, pulse, 120, and respirations, 26. This was not in keeping with the condition as shown by the roentgenogram and by the marked physical characteristics.

The roentgenographic appearance in this case is shown in figures 12 and 13. The vital capacity of the lungs was 1,500 cc. The white blood cells numbered 8,500 on January 20.

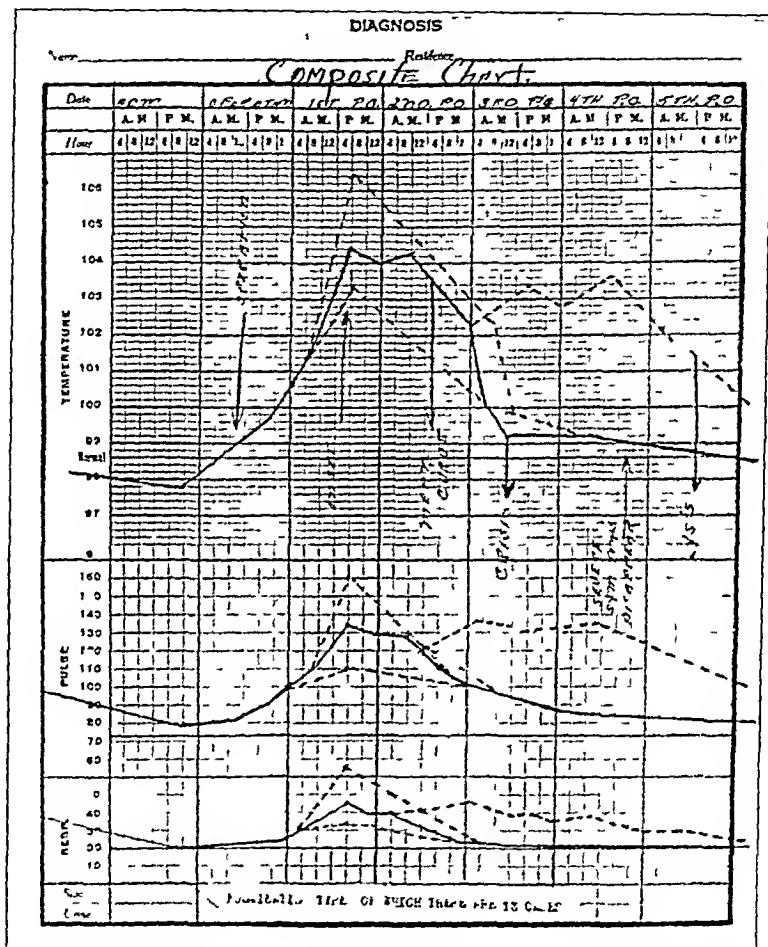


Fig 14—Composite chart of thirteen cases of the fulminating type of atelectasis

On January 22, the patient stated that he felt as though something had snapped in the chest, he spit up a large amount of mucopurulent material, and from then on experienced great relief and has felt no discomfort since.

CASE 36—A white woman, aged 36, was admitted to the hospital, Nov. 30, 1926. The diagnosis lay between ruptured appendix and pelvic peritonitis. Operation was performed the same day under gas (N_2O) and ether, a ruptured appendix was found with pus in the abdomen and involving the right tube and ovary. The abdomen was drained in three places and the patient was placed on Clark's peritonitis treatment. She was in a critical condition for about twelve days, she developed a phlebitis in the right leg on December 9.

The temperature was 101.6, pulse, 120, and respirations, 26, at the time of operation. A temperature of 105.4, pulse of 140, and respirations of 24, on December 2, gradually subsided to a temperature of 100.2, a pulse of 98, and respiration of 20 on December 8.

On the 10th the patient developed marked dyspnea, cyanosis and pain in the right side of the chest and began coughing. At this time, the temperature was 101.8, pulse, 110, and respiration, 36. On examination, the lower part of the right side of the chest was found to be limited in movement, with dullness to percussion, a distant breath sound, but no egophony or pectoriloquy was

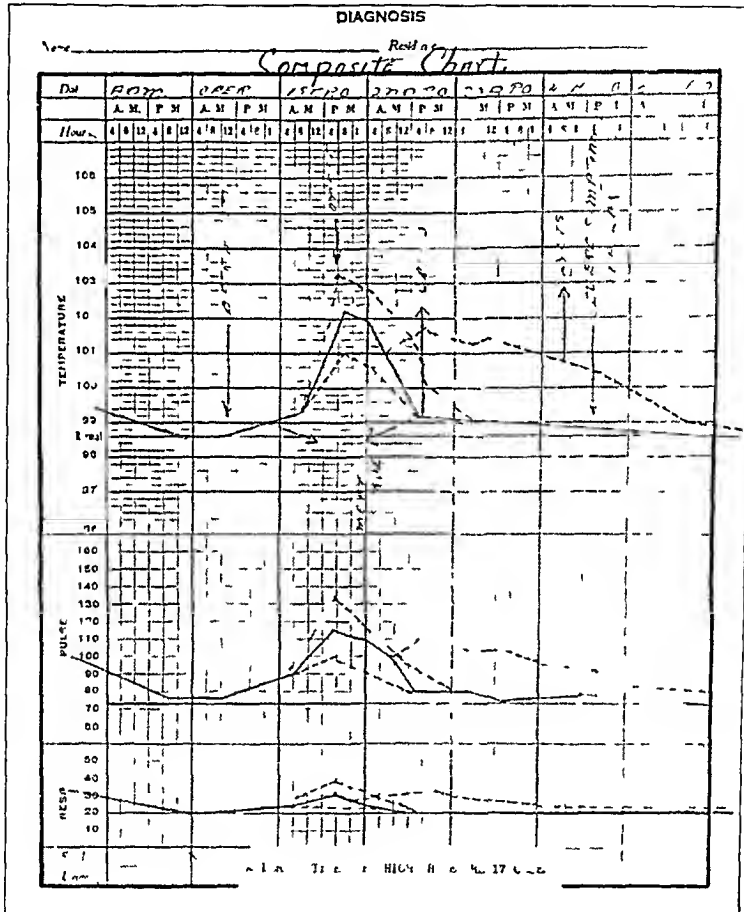


Fig 15—Composite chart of seventeen cases of moderate type of atelectasis

present, the mediastinal structures were pulled to the right, after ten hours a productive cough began and during the next few hours she spit up a large quantity of thick, mucopurulent, tenacious material. The chest was clear at the end of forty-eight hours, and the patient went on to an uneventful recovery.

CASE 37—A white man, aged 34, was admitted to the hospital, Feb 9, 1927. Bilateral herniorrhaphy was performed, February 10, under gas (N₂O) and ether, the duration of the anesthesia was one hour and fifty minutes. The day of the operation the temperature was 98.4, pulse, 72, and respirations, 18.

The following day, in the morning, he complained of considerable pain in the left side of the chest, no cough, diaphoresis or dyspnea were present. During

the evening and early morning, he became somewhat cyanotic, brick red erythema was present, and he complained of dyspnea. He began coughing at this time.

On February 12, the following physical signs were present: the patient was found lying on the left side, with the head averted, dullness and no breath sound were present over the lower part of the left lung, as well as inspiratory limitation of the left side of the chest, the patient was now cyanotic, and was perspiring freely.

Marked dyspnea was found when the patient was turned to the unaffected right side, only slight displacement could be made out.

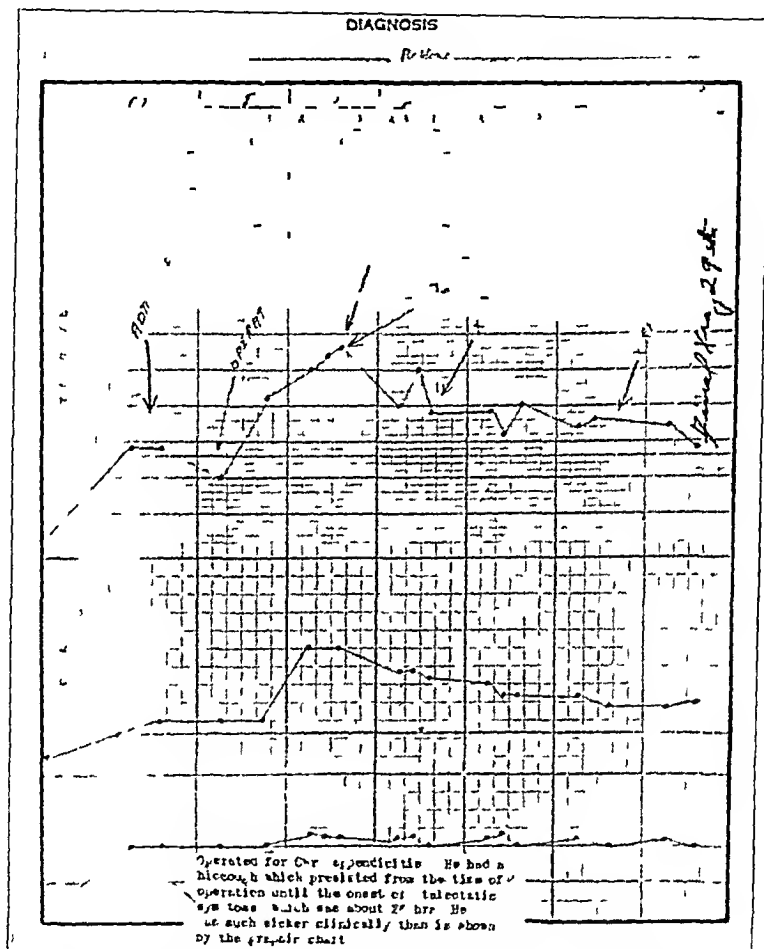


Fig 16 (case 35) —Summary of course of atelectasis

On February 13, he coughed up several mucus plugs, after which he felt greatly relieved. The chest was found to be entirely clear on February 17.

The roentgenograms were positive.

CASE 38—A white man, aged 52, was admitted to the hospital, Feb 3, 1927. A bilateral herniorrhaphy was performed, February 9, under gas (N₂O) and ether, the anesthesia lasted one hour and ten minutes. The temperature was 99, pulse, 76, and respirations, 20, on the day of the operation. During the day, after the recovery from the anesthetic, he complained of considerable mucus in the throat. On February 10 the patient complained of pain in the chest and an annoying, nonproductive cough. On examination, he was found to be perspiring freely, was somewhat cyanotic and was lying on the right side. Breath sounds

were diminished over the right base, dulness on percussion was found over this area, and there was only slight displacement of the heart and mediastinum to the right, he also had the typical brick red discoloration of the face and upper side of the chest and neck, shortly after, he began expectorating large amounts of thick, mucopurulent material. The temperature was 101.2, pulse, 94, and respirations, 26. After coughing and expectorating freely, the patient felt much relieved.

On February 12, the condition was found to be clear. The roentgenogram was positive.

CASE 39—A white man, aged 21, was admitted to the hospital, Jan. 25, 1927. The diagnosis was chronic appendicitis. Operation was performed the next day under gas (N₂O) and ether, the duration of the anesthesia was forty minutes. The appendix was removed, but no drain was inserted. The temperature was 98, pulse, 74, and respirations, 18, at the time of the operation, that afternoon, the temperature was 99.6, pulse, 90, and respirations, 22, due to the operation. Early the next day the patient had a nonproductive cough of an annoying type and complained of mucus in the throat, which he was unable to raise. The temperature was 100.4, pulse, 88, and respirations, 26. Although the temperature, etc., was not greatly increased, he nevertheless was somewhat cyanotic and perspired freely, there was also some displacement of the mediastinal structures, slight evidence of displacement of the trachea and a dull area over the lower part of the left lung with distant breath sign. The physical signs were not marked. The roentgenogram was positive for atelectasis.

CASE 40—A white woman, aged 29, was admitted to the hospital, Jan. 19, 1927. The diagnosis was acute cholecystitis. Operation was performed the following day under gas (N₂O) and ether. The gallbladder was found gangrenous and consequently was merely drained. The patient made a good recovery and was operated on again on January 28. At this time a cholecystectomy was performed under gas (N₂O) and ether. The following day the patient began perspiring profusely and complained of pain in the right side of the chest. She was moderately cyanotic and erythematous. The temperature was 99, pulse, 94 and respirations, 22, at the time of the operation. The following day the temperature was 101.8, pulse, 14, and respirations, 38. A few hours later she began coughing and spit up considerable thick, tenacious, mucopurulent material, after which she made an uneventful recovery. The pathologic change was limited to the right base, over which area the breath sounds were distant, and impairment to percussion was present.

CASE 41—A white woman, aged 22, was admitted to the hospital, Feb. 11, 1927. The diagnosis was chronic appendicitis. Operation was performed the following day under gas (N₂O) and ether. The duration of the anesthesia was one hour and ten minutes. Considerable difficulty was encountered, as the appendix was retroperitoneal. No drain was used. Early the following morning she complained of a choking sensation and much mucus in the throat, she became somewhat cyanotic and markedly erythematous about the face and neck with considerable diaphoresis. She began coughing early and spit up considerable thick, tenacious mucus. The temperature was 97.8, pulse, 84 and respirations 20, on the day of the operation. The following day, the temperature was 100.8, pulse, 116, and respirations, 30. The symptoms were localized in the right base, some dulness was present and the breath sound was absent. The chest was clear in about forty-eight hours.

CASE 42—A white man aged 22 was admitted to the hospital Feb. 20, 1927. The diagnosis was bilateral inguinal hernia. Operation was performed the

following day under gas (N_2O) and ether. The duration of the anesthesia was one hour and five minutes. The temperature was 98.4, pulse, 72, and respirations, 18, at the time of the operation, about twenty hours later the patient became moderately cyanotic and erythematous, with some diaphoresis. There was some evidence of pathologic change in the right base, distant breath sound and some impairment on percussion were present. These signs practically subsided in about forty-eight hours. The temperature was 100, pulse 104, and respirations, 28, on February 22. The symptoms had disappeared clinically by the following day.

CASE 43—A white woman, aged 66, was admitted to the hospital, Feb 8, 1927. The diagnosis was cholecystitis and cholelithiasis. Operation was performed, February 21, under gas (N_2O) and ether. The duration of the anesthesia was one hour and twenty minutes.

The temperature was 97.4, pulse, 86, and respirations, 22, at the time of the operation. The following day the patient was markedly cyanotic and erythematous and complained of considerable pain in the left side of the chest and difficulty in breathing, the left base was found to be impaired in movement and dull to percussion, distant breath sound and apex beat were present in the axillary line. The temperature was 101.2, pulse, 112, and respirations, 28. She began coughing shortly and spit up a thick, tenacious material rather copiously, the condition gradually cleared up, and the chest was normal five days later.

CASE 44—A white man, aged 56, was admitted to the hospital, Feb 10, 1927. The diagnosis was chronic cholecystitis and cholelithiasis. The patient was operated on February 17, under gas (N_2O) and ether, the duration of the anesthesia was one hour and fifteen minutes. At the time of the operation the temperature was 98.6, pulse, 76, and respirations, 20. Late the following afternoon the temperature was 100.8, pulse, 120, and respirations, 30, and the patient was definitely cyanotic and perspiring freely, with brick-red erythema of the face and neck. On examination, a definite dullness was found over the right base, especially posteriorly. There was diminished excursion of the right side of the chest. A roentgenogram taken, February 18, showed some displacement of the mediastinal structures. A roentgenogram taken the next day showed more evidence of collapse on the right side but also showed a patch of bronchopneumonia on the left. The final examination showed an almost normal chest. The condition cleared up rapidly, and on February 21, the chest was reported clear.

CASE 45—A white man, aged 38, was admitted to the hospital, Nov 25, 1926. Operation was performed on December 10 under drop ether, the anesthesia lasted for one hour and forty-five minutes, bilateral herniorrhaphy was done, and left indirect inguinal hernia, and recurrent inguinal hernia on the right were found. The temperature was 98.2, pulse, 76, and respirations, 18, at the time of the operation.

In the late afternoon of the 11th, he became cyanotic and dyspneic although the respiratory rate was not greatly increased, he had a persistent irritating, nonproductive cough. Physical examination revealed dullness in the right base, numerous rales above this area, no breath sound over the right base and marked limitation of movement of the right side of the chest. This condition persisted for about thirty-six hours, during which he spit up copious amounts of mucopurulent material, the chest had returned to normal in about forty-eight hours although he had an irritating cough for about twenty-four hours longer. The fastigium showed a temperature of 101.4, pulse, 94, and respirations, 26.

The patient made an uneventful recovery from the 14th to the time of discharge.

The following five cases were of the evanescent type.

EVANESCENT TYPE

CASE 46—A white man, aged 24, was admitted to the hospital, Feb 7, 1927. The diagnosis was bilateral inguinal hernia. Operation was performed the following day under gas (N_2O) and ether, the duration of the anesthesia was one hour and five minutes. The temperature was 96.4, pulse, 86, and respirations, 20, on the day of the operation. About twenty-six or twenty-eight hours later, he was moderately cyanotic, with some erythema of the face and neck and moderate diaphoresis, the cough was almost immediately productive, and he spit up considerable yellowish, tenacious material. The attack began suddenly, with pain

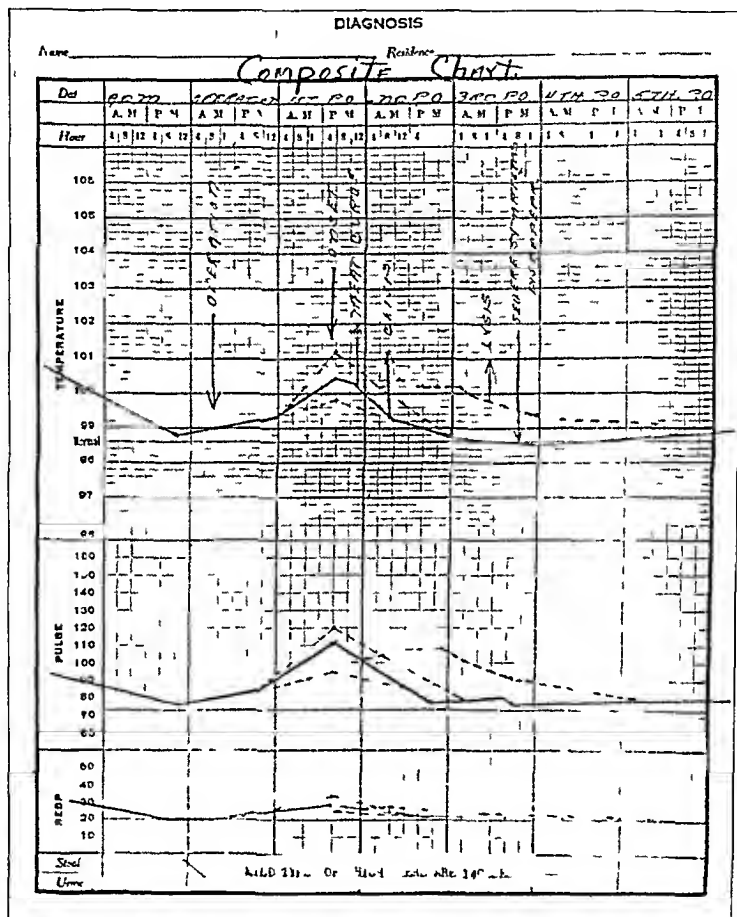


Fig. 17—Composite chart of fourteen cases of the mild type of atelectasis

in the upper part of the left side of the chest, in which a slight dulness on percussion and distant breath sound were present About twenty-four hours later, all signs had disappeared The temperature was 101, pulse, 100, and respirations, 26, on February 9

CASE 47—A white man, aged 46, was admitted to the hospital, Feb 6, 1927. The diagnosis was bilateral indirect inguinal hernia. The patient was operated on the following day, and bilateral Bassini herniorrhaphy was done. The anesthesia lasted fifty-five minutes. Gas (N₂O) and ether were given. The temperature was 98.4, pulse 84 and respirations, 20 at the time of the operation. The patient was apparently making a good recovery until the early morning of

TABLE 1—Summary of Fifty Case Histories

Case	Age	Type	Operations	Onset	Regression
1	17	Fulminant	Appendectomy	26 hours	Crisis
2	22	Fulminant	Appendectomy	26 hours	Lysis
3	17	Fulminant	Appendectomy	30 hours	Crisis
4	28	Fulminant	Cholecystectomy	64 hours	Complication, peritonitis hepatitis
5	55	Fulminant	Cholecystectomy	30 hours	Complication lobar pneumonia
6	22—	Fulminant	Appendectomy	32 hours	Lysis
7	28	Fulminant	Appendectomy	20 hours	Lysis
8	28	Fulminant	Perineorrhaphy	16 days	Lysis
9	41	Fulminant	Herniorrhaphy	20 hours	Lysis
10	16	Fulminant	Appendectomy	18 hours	Lysis
11	12	Moderate	Appendectomy	30 hours	Crisis
12	21	Moderate	Herniorrhaphy	30 hours	Crisis
13	13	Moderate	Herniorrhaphy	36 hours	Lysis
14	15	Moderate	Herniorrhaphy orchiectomy	36 hours	Lysis
15	28	Moderate	Appendectomy	28 hours	Lysis
16	39	Moderate	Appendectomy	20 hours	Lysis
17	36	Moderate	Appendectomy	28 hours	Complication peritonitis
18	10	Moderate	Herniorrhaphy (bilateral)	24 hours	Lysis
19	61	Moderate	Herniorrhaphy (right)	30 hours	Lysis
20	68	Moderate	Appendectomy	72 hours	Lysis
21	40	Moderate	Gastro enterostomy	28 hours	Lysis
22	14	Moderate	Cholecystectomy	26 hours	Lysis
23	25	Moderate	Appendectomy, suspension	24 hours	Lysis, bronchitis
24	30	Moderate	Cholecystectomy	30 hours	Lysis
25	36	Mild	Appendectomy	26 hours	Crisis
26	38	Mild	Herniorrhaphy	28 hours	Lysis
27	42	Mild	Appendectomy	10 days	Lysis
28	21	Moderate	Appendectomy	28 hours	Lysis
29	52	Mild	Herniorrhaphy (right)	26 hours	Crisis
30	34	Mild	Herniorrhaphy (bilateral)	24 hours	Lysis
31	66	Mild	Herniorrhaphy	24 hours	Lysis
32	34	Mild	Perineorrhaphy herniorrhaphy (femoral)	30 hours	Lysis
33	22	Mild	Appendectomy	24 hours	Lysis
34	29—	Mild	Cholecystectomy	18 hours	Lysis
35	24	Mild	Sigmoidectomy	14 hours	Lysis, complication bronchitis
36	27	Mild	Appendectomy	26 hours	Lysis
37	55	Mild	Cholecystectomy	28 hours	Lysis
38	24	Vanescant	Herniorrhaphy	28 hours	Crisis
39	16	Vanescant	Herniorrhaphy	36 hours	Lysis
40	12	Vanescant	Appendectomy	18 hours	Crisis
41	18	Vanescant	Appendectomy	12 hours	Crisis
42	43	Vanescant	Cholecystectomy	18 hours	Lysis
43	23	Mild	Herniorrhaphy	20 hours	Lysis
44	32	Fulminant	Appendectomy	28 hours	Crisis
45	65	Mild	Cholecystectomy	18 hours	Lysis
46	18	Moderate	Herniorrhaphy	14 hours	Lysis
47	10	Fulminant	Appendectomy	18 hours	Crisis
48	35	Moderate	Appendectomy suspension	14 hours	Lysis (18 hours)
49	21	Moderate	Appendectomy	16 hours	Lysis
50	47	Fulminant	Cholecystectomy	16 hours	Lysis

* N₂O—Ether is understood to mean a gas induction which was followed by the use of ether vapor. Ben Morgan apparatus and the new type of McKesson machine were used.

† In this column ♂ indicates male ♀ female.

‡ This case was a true lobar pneumonia from the onset, no operative procedure previously

TABLE 1—Summary of Fifty Case Histories—Continued

Case	Location	Deaths	Anesthetic	Sex†	Disappearance Time	
					Clinical Signs	Physiologic Signs
1	Right base	No	N ₂ O—Ether*	♂	36 hours	60 hours
2	Right base	No	N ₂ O—Ether	♂	60 hours	5 days
3	Right base	No	N ₂ O—Ether	♀	36 hours	60 hours
4	Left base	Yes	Drop ether	♀	Expired (peritonitis and myoeriditis)	
5	Right upper lobe	Yes	Local procaine, 1%, field block	♀	Expired (Bronchopneumonia and sepsis)	
6	Right base	No	N ₂ O—Ether	♀	3 days	5 days
7	Right middle and base	No	N ₂ O—Ether	♂	6 days	13 days
8‡	Right middle and base	No	Postpneumonic	♂	Still showed pathologic condition on leaving hospital	
9	Right upper lobe	No	N ₂ O—Ether	♂	3 days	7 days
10	Right middle and base	No	N ₂ O—Ether	♂	2 days	4 days
11	Left base	No	Drop ether	♀	36 hours	48 hours, except the heart still to left
12	Left upper lobe	No	N ₂ O—Ether	♂	48 hours	60 hours
13	Left base	No	N ₂ O—Ether	♂	36 hours (1st) 72 hours (2d)	8 days in all
14	Right upper and base	No	Drop ether	♂	50 hours	72 hours
15	Right base	No	N ₂ O—Ether	♂	5 days	9 days
16	Right base	No	N ₂ O—Ether	♂	3 days	10 days
17	Left base	Yes	N ₂ O—Ether	♀	Expired (general peritonitis)	
18	Right middle and base	No	Local procaine, 1%, block	♂	5 days	7 days
19	Right base	No	N ₂ O—Ether	♂	5 days	7 days
20§	Right base	Yes	Spinal 10 cc 1% procaine	♂	Cleared up then developed pneumonia in left lung and general peritonitis	
21	Right middle and base	No	N ₂ O—Ether	♂	3 days	5 days
22	Right upper and base	No	N ₂ O—Ether	♀	4 days	7 days
23#	Right base	No	N ₂ O—Ether	♀	5 days	8 days
24	Left base	No	N ₂ O—Ether	♀	3 days	5 days
25	Right middle and base	No	N ₂ O—Ether	♂	48 hours	72 hours
26	Left base	No	Drop ether	♂	36 hours	60 hours
27	Right base	No	N ₂ O—Ether	♀	36 hours	60 hours
28	Left base	No	N ₂ O—Ether	♂	24 hours	48 hours
29	Right base	No	N ₂ O—Ether	♂	36 hours	60 hours
30	Left base	No	N ₂ O—Ether	♂	2 days	5 days
31	Right base	No	Local block procaine 1%	♀	2 days	4 days
32	Left base	No	N ₂ O—Ether	♀	2 days	5 days
33	Right base	No	N ₂ O—Ether	♀	2 days	4 days
34	Right base	No	N ₂ O—Ether	♀	4 days	8 days
35	Right base	No	N ₂ O—Ether	♀	4 days	8 days
36	Right base	No	N ₂ O—Ether	♂	36 hours	48 hours
37	Right base	No	N ₂ O—Ether	♂	3 days	6 days
38	Left upper lobe	No	N ₂ O—Ether	♂	18 hours	36 hours
39	Right base	No	N ₂ O—Ether	♂	18 hours	28 hours
40	Right base	No	N ₂ O—Ether	♂	18 hours	28 hours
41	Right base	No	N ₂ O—Ether	♀	36 hours	48 hours
42	Right base	No	N ₂ O—Ether	♂	24 hours	36 hours
43	Right base	No	N ₂ O—Ether	♂	36 hours	48 hours
44	Right base	No	N ₂ O—Ether	♂	40 hours	72 hours
45	Left base	No	N ₂ O—Ether	♀	48 hours	4 days
46	Bilateral	No	Spinal 1% 10 cc procaine	♂	72 hours	5 days
47	Right middle and base	No	Procaine and E ₁ s	♂	48 hours	4 days
48	Left upper	No	N ₂ O—Ether	♀	48 hours	4 days
49	Right base	No	N ₂ O—Ether	♀	50 hours	4 days
50	Right middle and base	No	N ₂ O—Ether	♀	72 hours	5 days

§ This patient was operated on under spinal anesthesia, developed a collapse which cleared up entirely but subsequently developed a bronchopneumonia on the left in conjunction with a peritonitis.

This patient developed a purulent bronchitis after the collapse had entirely disappeared.

the 9th, when he suddenly became cyanotic, dyspneic and began coughing, complaining of pain in the chest at the same time. Physical examination revealed some dulness in the right base with distant breath sound. During the night, he spit up considerable thick, tenacious mucopurulent material, and in the morning roentgen-ray evidence was negative but still showed a few rales. Two days later the chest was found to be entirely clear.

CASE 48—A white boy, aged 12, was admitted to the hospital, Feb 14, 1927. The diagnosis was subacute appendicitis. Operation was performed the following day under drop ether, the anesthesia lasted thirty minutes. At the time of the

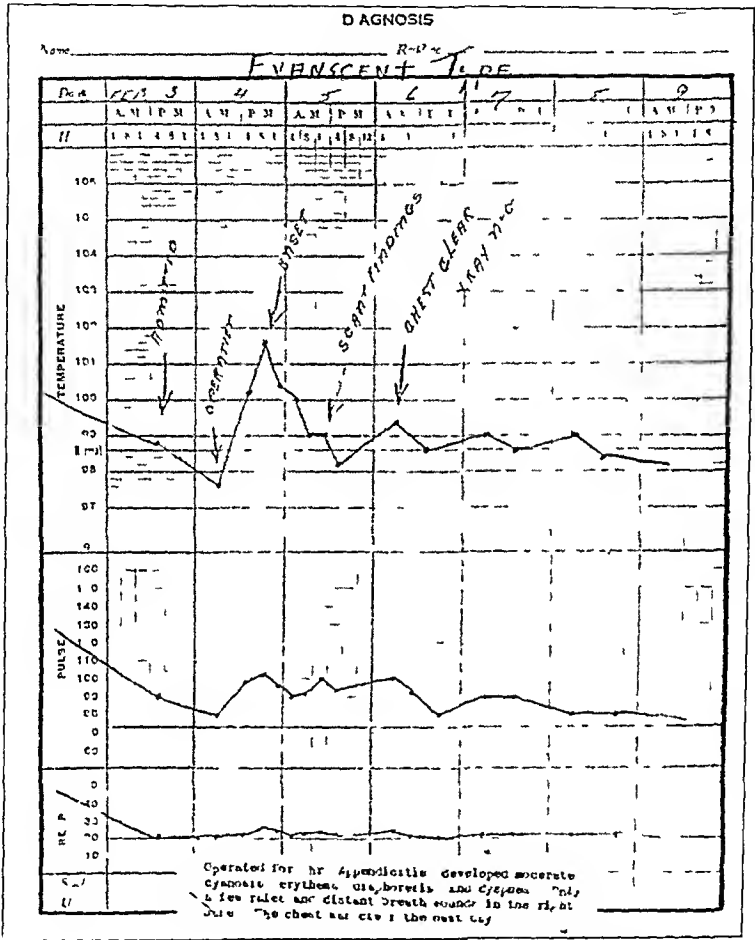


Fig 18 (case 49) —Summary of course of atelectasis

operation the temperature was 98.4 pulse 86 and respirations 22. The patient apparently was doing nicely until the early morning of February 16, when he became somewhat cyanotic and dyspneic and had facial erythema. The temperature was 100.6, pulse 104, and respirations, 30. On examination that morning the breath sounds were found suppressed on the right and there was some limitation of motion in the right side of the chest.

He expectorated some plugs and a moderate amount of thick, tenacious material. The following day the chest was reported as clear. A roentgenogram on February 27 showed a normal chest.

CASE 49—A white girl, aged 18, was admitted to the hospital, Feb 7, 1927. She was operated on the next day under drop ether, open method. The anesthesia lasted for thirty-five minutes. The temperature was 98.8, pulse, 86, and respirations, 18, the day of the operation. The night of the following day and early in the morning, the temperature was 101.8, pulse, 102, and respirations 26. A profuse diaphoresis was present, and the patient complained of tightness in the chest. She coughed very little. The next morning, nothing but a few rales was present in the right base. She expectorated several times during the day, and was somewhat erythematous. Nothing else of importance could be found.

The patient went on to an uneventful and smooth recovery.

Cholecystectomy was performed, January 27, under spinal anesthesia. Difficulty was encountered, and closure was effected under gas (N₂O) anesthesia.

CASE 50—A white man, aged 43, was admitted to the hospital, Jan 25, 1927, which lasted fifteen minutes. About sixteen hours later there was a sudden rise in the temperature to 100.8, the pulse rate was 114, respirations, 26, and there was some feeling of tightness in the throat and chest. Considerable diaphoresis and some erythema and cyanosis were present, the next day, a few rales were heard in the right side of the chest, there was suppression of the breath sounds in the lower part of the right side of the chest.

The patient coughed up considerable thick, mucopurulent material and felt relieved. The next day about the same symptom complex was present, but the condition cleared up in about twenty-four hours. The temperature was 102.4, pulse, 120, and respirations, 28, the second time at 11 p. m. The chest was found to be clear the next day.

Roentgen-ray examination showed only suggestive displacement of the heart and mediastinal structures to the right.

GLOSSOPHARYNGEAL NEURALGIA (TIC DOULOUREUX)

ITS DIAGNOSIS AND TREATMENT *

WALTER E DANDY, MD

BAITIMORE

The pain of trigeminal neuralgia was for many years considered so distinctive in type and severity as to deserve the restrictive designation, "tic douloureux" Why this particular nerve should alone be subject to this paroxysmal, ticklike type of pain and all the other cranial and spinal sensory nerves be seemingly immune, has never had a rational explanation

As a matter of fact, pain of the same type does occur in the distribution of the glossopharyngeal nerve, so that the term "tic douloureux" is no longer synonymous with trigeminal neuralgia, but must now include glossopharyngeal neuralgia Whether similar pains of the facial, vagus and possibly of other sensory nerves will eventually be found to be of similar kind, remains to be seen

Weisenburg¹ was apparently the first to direct attention to the resemblance of an unusual pain of the ninth nerve to the so-called idiopathic pain of tic douloureux of the trigeminal nerve In his patient, however, the paroxysms of pain were caused by a tumor in the cerebellopontile angle, but in many ways the pain was analogous to that of tic douloureux of the trigeminal nerve In fact, it was first mistaken for trigeminal neuralgia, but the pain was not influenced by a partial removal of the gasserian ganglion The pain was always at the "root" of the tongue, and extended down the throat and to the ear There was a burning feeling and dryness in the throat, and frequently the sensation of flies and roaches crawling At times the paroxysms were excruciating, and usually were brought on by eating During the last year of the patient's life, contact of food with a sharply defined trigger zone at the base of the tongue caused terrific paroxysms of pain Actual chewing movements did not induce this pain

Ten years after Weisenburg's report, three cases of "algie velopharyngee essentielle" were described by Sicard and Robineau In each case the pain was paroxysmal, was induced by swallowing chewing speaking and often spontaneously, and was referred to one side of the pharynx, soft palate and tonsil Doubtless because the pain was of

* From the Johns Hopkins Hospital and University

1 Weisenburg T H Cerebello-Pontile Tumor Diagnosed for Six Years as Tic Douloureux The Symptoms of Irritation of the Ninth and Twelfth Cranial Nerves J A M A 54 1600 (May 14) 1910

2 Sicard R and Robineau Communications et presentations I Algie velopharyngee essentielle Traitement chirurgical Rev neurol 36 256 1920

long duration and not accompanied by other manifestations of tumor the condition was considered to be "essential" or idiopathic. It is hardly probable that they recognized the pain as an involvement solely of the glossopharyngeal domain, for their treatment, as practiced and recommended, consisted in sectioning in the neck the branches of the glossopharyngeal nerve, the pharyngeal branches of the vagus and the superior cervical ganglion. Since the appearance of these publications, a number of cases have accumulated rapidly.

Doyle³ reported four and Adson⁴ three other cases from the Mayo Clinic. Harris,⁵ in his splendid book, "Neuritis and Neuralgia," adds six cases from his own service in London. As this paper was written another case was appended by Goodyear.⁶

Although all of these have been reported as cases of glossopharyngeal neuralgia, the doubt lurks that the pain is confined exclusively to the distribution of the glossopharyngeal nerve. For this reason, the suggested treatment of Sicard and Robineau was followed in the cases of Doyle and Adson, i. e., the branches of both the vagus and glossopharyngeal nerves were divided. They seem to have been misled by an uncertainty of the sensory nerve supply to the pharynx, believing branches of the sphenopalatine ganglion and vagus nerve to be the source of its supply. Harris is "uncertain whether the vagus has any share in the production of this (glossopharyngeal) neuralgia, and whether section of the pharyngeal branch of the vagus is also necessary." It appears probable that the unorthodox and faulty conclusions by Vernet⁷ (referred to by Sicard and Robineau and by Doyle) on the nerve supply to the pharynx by the glossopharyngeal and vagus nerves is largely responsible for this confusion. The sensory distribution of the ninth nerve will be considered later.

In addition to the foregoing series of cases assembled from the literature, two more are reported. Curiously, these cases appeared six weeks apart. Both were recognized as glossopharyngeal neuralgia by the characteristic history of the attacks before the patients were actually seen. These cases are presented not only to emphasize the clinical picture of this remarkable and not uncommon condition, but also to present a simple form of treatment, practically devoid of danger, and productive of permanent cure without disability.

3 Doyle, J. B. A Study of Four Cases of Glossopharyngeal Neuralgia, *Arch. Neurol. & Psychiat.* **9** 34 (Jan.) 1923.

4 Adson, A. W. The Surgical Treatment of Glossopharyngeal Neuralgia, *Arch. Neurol. & Psychiat.* **12** 487 (Nov.) 1924.

5 Harris, W. *Neuritis and Neuralgia*, New York: Oxford University Press, 1926.

6 Goodyear, H. M. Tic Douloureux of the Glossopharyngeal Nerve. *Arch. Otolaryng.* **5** 341 (April) 1927.

7 Vernet, M. Syndrome du trou déchiré postérieur (Paralysie des nerfs glossopharyngien, pneumogastrique spinal). *Rev. Neurol.* **34** 117 1918.

CASE 1—History—A strong, healthy man, aged 45, but looking much older, was first seen in the neurologic dispensary by Dr Frank Ford, who at once recognized the pain to be that of glossopharyngeal neuralgia. Seldom have we seen a man in greater agony, even in the most severe cases of trigeminal neuralgia. He was then having paroxysms of terrific pain in rapid succession, some induced by swallowing or talking and some even occurring spontaneously. Afraid to swallow or to talk, he sat in terror, with his head hanging forward and directed toward the right in order to allow the saliva to drool from his mouth and away from the affected side. He dared to eat only after his tongue had been cocaineized over its base, and particularly, as he so strongly emphasized, over one spot about the size of a dime, near the junction of the tongue with the left tonsil. This "trigger zone," so real to him, did not show anything on examination. For three and one half years he had endured this pain at varying intervals. It had begun in September, 1923, with a severe knifelike thrust at the base of the tongue immediately after taking a drink of cold water, it lasted a few seconds, but for three weeks it occurred several times a day and ended as abruptly as it began. During the attacks, the left ear drum felt as though it were being pushed out and "were ready to burst." In one severe attack just before his operation, the patient felt as if all the teeth in the lower jaw on the affected side were "jumping out of their sockets." For more than two years he was free from pain when asleep, but during the six months before admission to the hospital, he had been frequently wakened from a sound sleep by the knifelike pains, particularly when lying on the left side. The attacks were due, he thought, to the accumulation of saliva on the trigger zone. His tonsils had been removed in September 1926, and again in November 1926, in the vain hope of effecting a cure. During the latter operation, the throat was extensively burned with a cautery. The pain was decidedly worse afterward, and from then until his admission to the Johns Hopkins Hospital in April, 1927, the pains became more and more frequent and severe. He said it seemed to him that a red hot poker was being jabbed through the tongue. At first the attacks were of only two or three seconds' duration, but during the past six months each had lasted about ten seconds. He had the impression that the attacks were more frequent when he talked a great deal, but in his occupation as a missionary there was little opportunity to get complete rest for any length of time. He had obtained relief for a few days by local application of cocaine.

Results of all examinations, including tests for taste and sensation in the domain of the ninth nerve, were entirely negative. The Wassermann reaction was negative.

Operation—On April 6, 1927, I performed an intracranial section of the ninth nerve, in the posterior cranial fossa (fig 1). The patient made an uneventful recovery, with immediate and subsequent complete relief from pain of any kind. There was no disturbance of swallowing afterward. He was unable to detect any symptoms due to the loss of function of the ninth nerve. Objectively, however, there was total loss of sensation and of taste over the back of the tongue and pharynx (fig 6, 7 and 8). No motor impairment of any kind could be detected by examination.

CASE 2—A man, aged 56, well developed and strong, but pale and sallow from lack of nourishment, was referred by my associate, Dr S J Crowe, on May 10, 1927. Fifteen years before, while talking with a friend, the patient had been suddenly seized with an excruciating pain in a spot at the back of the tongue and near the right tonsil. It lasted only a few seconds, but during the following years similar pains in the same location struck him suddenly without warning,

after they had disappeared, he was entirely free of pain. It seemed as though a red hot iron were being thrust through the tongue at this spot. At first he was unable to discover any inciting cause for the attacks. The free intervals were as long as a year and a half, but the pain always recurred in the same spot. Since November, 1926, the attacks had become more frequent and severe and of longer duration, often lasting several seconds. During this time, the attacks have been induced consistently by drinking, eating and talking. For two weeks before I saw the patient, he had been almost without food or drink and had scarcely dared to speak. Sneezing and coughing also brought on the paroxysms. For the two days before he consulted me, one attack had followed almost immediately

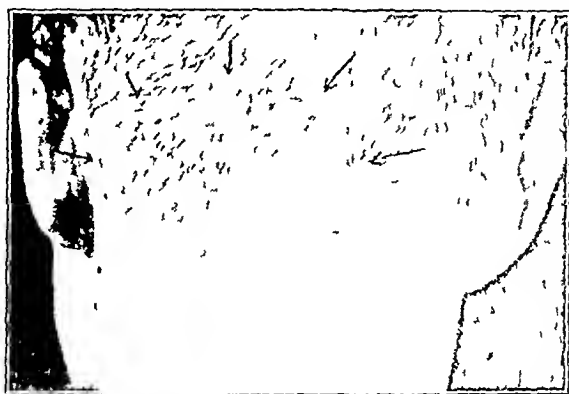


Fig 1—Posterior view of patient's head to show the operative scar, indicated by the arrows. The photograph was taken on discharge from the hospital ten days after the operation.

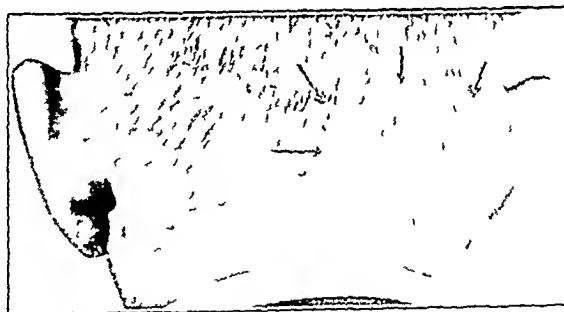


Fig 2—Scar of second patient when ready for discharge two weeks after operation. The arrows indicate the position of the scar.

on the other, giving the patient almost no interval of relief longer than a few minutes, despite hypodermic injections of morphine. During my brief examination the patient had three paroxysms, each lasting about five seconds. Immediately after each attack, he could swallow with impunity for a few seconds, but this period of immunity was soon over. He could direct the examiner to the spot on the base of the tongue which seemed to him so well defined but nothing was objectively evident. Results of all examinations, including tests for taste and sensation, in the distribution of the ninth nerve were negative.

Operation—On May 11, 1927 under local procaine hydrochloride anesthesia the glossopharyngeal nerve was divided intracranially in the lateral cistern (fig 2). Postoperative convalescence was uneventful. All pain immediately dis-

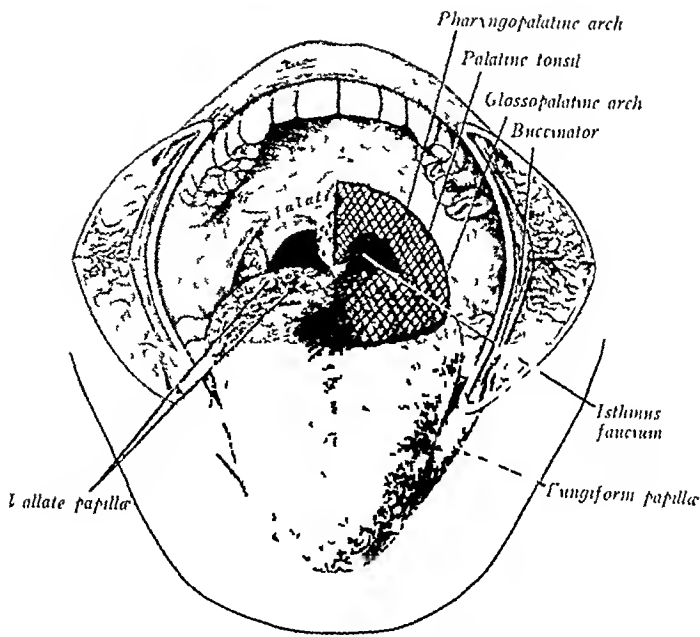


Fig 3—Area of anesthesia in the mouth following unilateral division of the glossopharyngeal nerve (Photograph from Gray's "Anatomy")

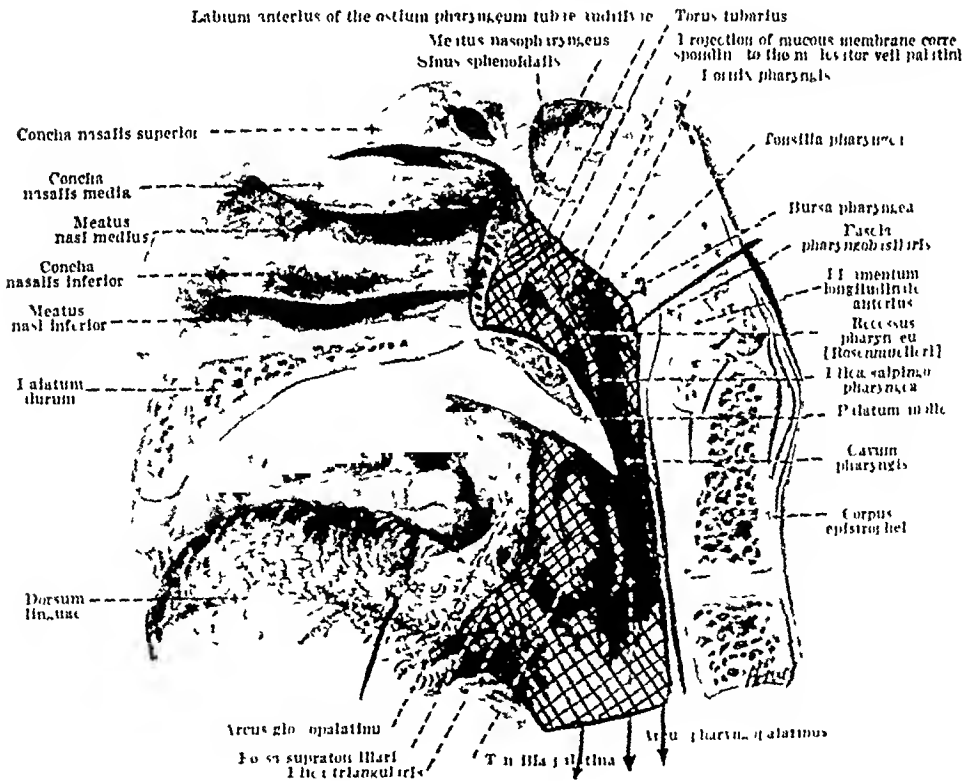


Fig 4—Cross-hatched area indicates area of anesthesia in the pharynx and nasopharynx lateral view. Sensation is uncertain in the area shown in dots: the vault of the pharynx (Photograph from Spitzholz)

appeared and had remained absent up to June 1, 1927. The patient was unable to detect any abnormal sensations incident to the loss of sensation. There were no signs or symptoms of injury to the vagus nerve. The accompanying illustrations, figures 3, 4 and 5, show the sensory changes due to the loss of the ninth nerve. Motor loss could not be observed. The patient was a public speaker, and, despite his terrible pain, was most reluctant to have anything done unless assured that his voice would be unimpaired, there was no change.

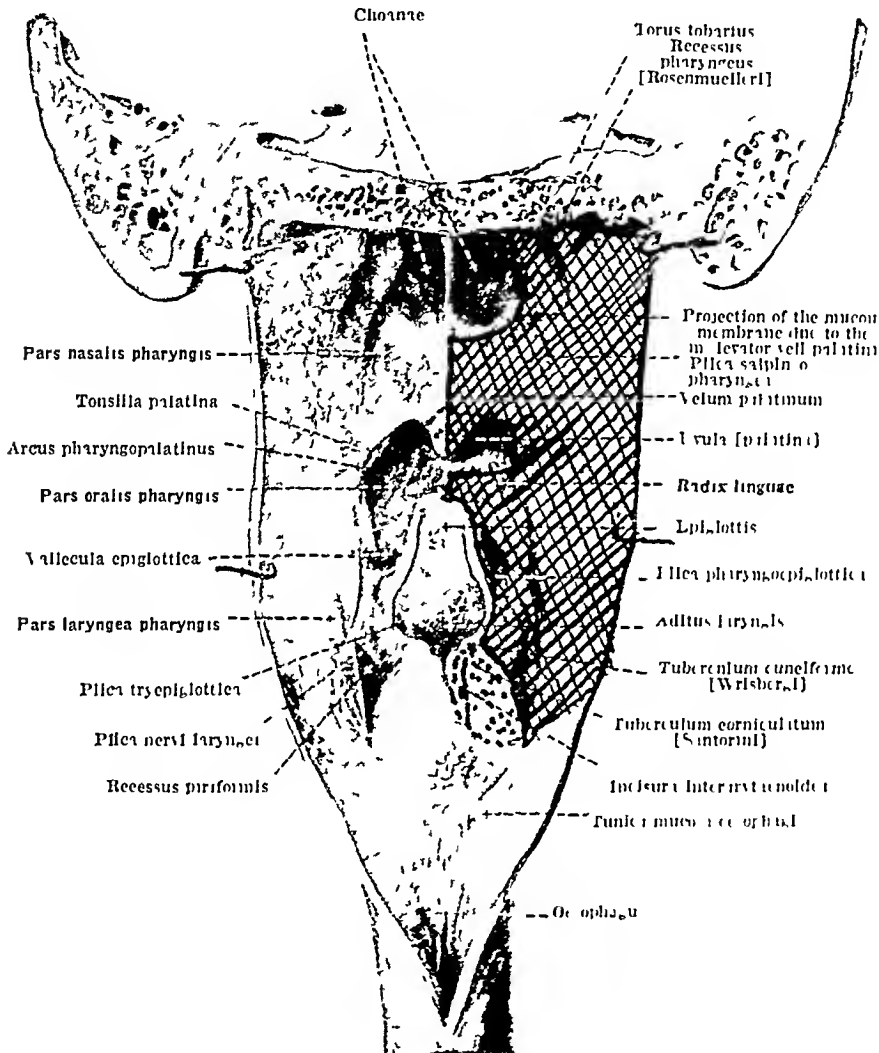


Fig 5—Showing area of anesthesia in the pharynx (looking from behind) after division of the glossopharyngeal nerve. Sensation is uncertain in the area over the esophagus, shown in dots. (Photograph from Spalteholz.)

THE OPERATION

The glossopharyngeal nerve is divided intracranially, a unilateral cerebellar approach being used. It is the same exposure that I have used for the past three years as the method of choice in dividing the sensory root of the trigeminal nerve. The glossopharyngeal nerve is however much easier of access. It is one of the simplest of intracranial operations and can readily be performed with

either local or general anesthesia. An incision is made which begins at a point about 2 centimeters below theinion, gently curves upward, reaching slightly above the line of attachment of the trapezius muscle to the occipital bone, and then turns more abruptly downward along the mastoid bone until within from 1.5 to 2 centimeters of its tip (fig 6). The trapezius muscle is divided just below its attachment and retracted downward and outward. The bone is removed over much of the corresponding side, at least far enough to the midline to afford access to the cisterna magna, which is punctured to release fluid and to provide additional room. The bone is rongeuired laterally to the mastoid, but not far enough to enter the mastoid cells. The dura is opened in stellate fashion. Gentle elevation of the cerebellar lobe then allows ample exposure of the cerebellopontile angle. The cisterna lateralis is quickly brought into view, and, when pricked, the lining arachnoid membrane collapses (fig 7). The fifth, eighth, ninth, tenth and

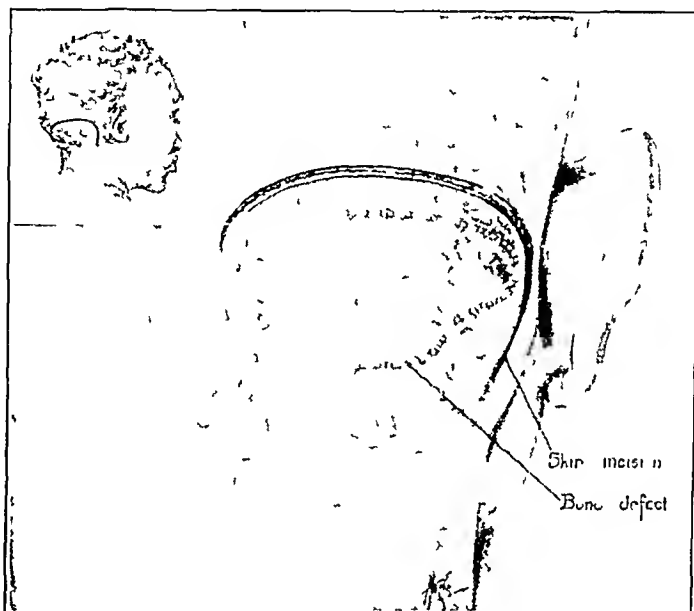


Fig 6—Outline of incision in skin and defect in bone in operation for intracranial section of the glossopharyngeal nerve

eleventh cranial nerves then appear. The auditory nerve is probably the best landmark. The glossopharyngeal nerve is, of course, next in succession in a caudal direction and is probably from 0.75 to 1 centimeter caudal to the auditory nerve. A relatively tiny nerve, about the size of the lead in a pencil, always single and free from contact with the vagus, which lies immediately caudal—the glossopharyngeal nerve—can be readily lifted with a blunt hook without touching the vagus or any other nerve. A knife or a pair of scissors cuts the suspended nerve in an instant (fig 8). The patient whose nerve was sectioned under procaine hydrochloride anesthesia (applied only extracranially) did not experience any sensation when the glossopharyngeal nerve was divided. The operation should be devoid of danger. There is no reason for even touching the vagus, auditory or facial nerves. There can, of course, be no question about the permanency of a cure, for precisely the same problem has long since been solved in trigeminal neuralgia. After section of the sensory root of any nerve central to its ganglion, regeneration is impossible.

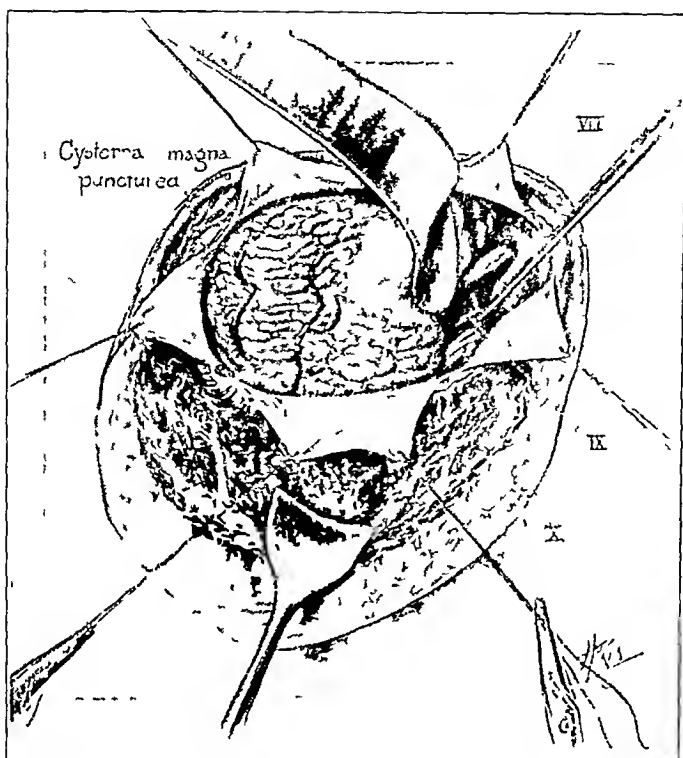


Fig 7—Elevation of the cerebellum, exposing the cerebellopontile angle after puncture of the cisterna magna and the cisterna lateralis. The ninth nerve is shown drawn forward with the knife hook. The eighth and tenth nerves are always plainly in view. The ninth nerve is separated from the vagus by 2 or 3 mm, thereby preventing any injury to the vagus during its manipulation and division.

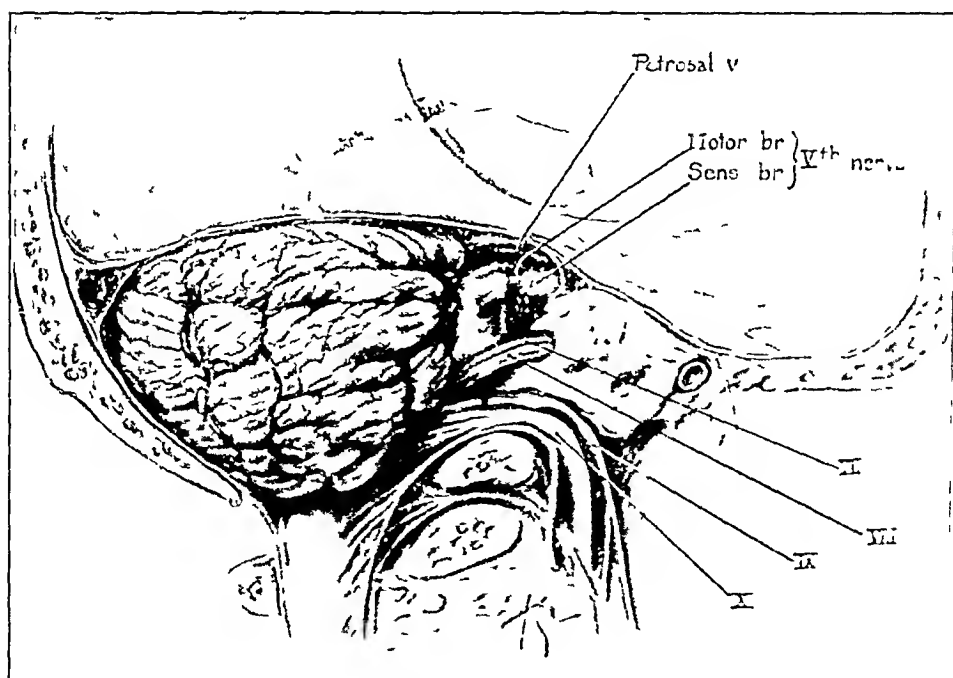


Fig 8—Point of division of the glossopharyngeal nerve intracranially. In the same exposure the fifth nerve may be divided in trigeminal neuralgia without injury to the motor branch, which is a few millimeters distant.

The operations heretofore employed in glossopharyngeal neuralgia have been of the peripheral type, either section or avulsion of the nerve. Besides the local difficulties of isolating and dividing the ninth nerve high up in the neck without injuring the sympathetic trunk and particularly the vagus (a difficult task), the objection remains that regeneration of the nerve is likely to follow its division peripherally. As noted before, Sicard and Robineau introduced this manner of division of the nerve for glossopharyngeal neuralgia, and in all cases the sympathetic and pharyngeal fibers of the vagus were intentionally included. Adson avulsed the glossopharyngeal nerve in the hope that at least the petrous ganglion would be included, but the vagus, being closely associated, was injured. He regretted that he had not tried intracranial section of the nerve and hoped to do so in his next case. In a patient afflicted with an extensive carcinoma of the tongue and pharynx, Fay,⁸ in 1926, sectioned the ninth nerve, together with three upper cervical nerves, in an extensive occipital and cervical exposure. The vagus nerve was injured, and, doubtless because of inadequate exposure, the pulse rate immediately dropped from 125 to 80. He also planned a unilateral cerebellar approach if a patient with glossopharyngeal tic douloureux should come for operation. Harris, in 1926, attempted to inject the glossopharyngeal nerve (in the neck) with alcohol, but failed to reach the nerve. Injections of alcohol could hardly be successful. Injury to the contiguous jugular vein, the internal carotid artery, the sympathetic, spinal accessory and vagus nerves would seem more probable than a successful injection into the glossopharyngeal nerve.

In passing, it is well to note the importance of section of the glossopharyngeal nerve in inoperable carcinomas of the tonsil and nasopharynx. Should the domain of the fifth nerve also be invaded by the growth, the sensory root of the trigeminal nerve can easily be divided at the same time and with little added time. As mentioned before, this approach has been my method of choice for section of the sensory root in tic douloureux for the past few years.

CLINICAL FEATURES

The close similarity between glossopharyngeal neuralgia and tic douloureux of trigeminal origin has been commented on by Sicard and Robineau, Doyle, Adson and Harris. Surely both varieties of this fearful pain equally deserve the appellation, tic douloureux. The characteristic sudden, ticlike paroxysms of excruciating pain and the induction of pain by external stimuli are common to each.

In the twenty cases of glossopharyngeal neuralgia assembled from the literature and epitomized in the accompanying table, the clinical picture is strikingly uniform. The paroxysms of pain always strike some part of the glossopharyngeal sensory area—the tonsil, back of the tongue or the pharynx, the pain is always unilateral and induced by liquids or solids passing over the sensory endings of the ninth nerve in the mouth or pharynx. The pain is always excruciating, it is variously described as lancinating, knifelike or like stabs of a red-hot iron. Each individual pain usually lasts only a few seconds, rarely over a

⁸ Fay, T. Intracranial Division of Glossopharyngeal Nerve Combined with Cervical Rhizotomy for Pain in Inoperable Carcinoma of the Throat. *Ann Surg* 84:456, 1926.

minute, the duration of the paroxysm, is, therefore, usually less than that of trigeminal neuralgia, but it would seem more severe, if possible. There is a strong tendency for the paroxysms to occur in a series over a period of time varying from a few days to a few weeks, in nearly every case intermissions of several months have occurred. The longest period of relief was three and three-fourths years in one of Adson's cases. But the identical pain always returns in precisely the same location. In a few cases there has been some tendency for the pain to shift from an initial point more remote and eventually to reach the central area of the glossopharyngeal sensory domain, for example, in two of Doyle's cases the original pain was in the ear, and in one of Adson's cases it was in the lobule of the ear and the angle of the mandible, but the pains were brought on by swallowing or other stimuli of the tongue and pharynx. In nearly all cases pain radiates to the ear, i. e., the meatus, the concha, the lobule or in front of or behind the ear, and not infrequently it begins there either before the more central pain or almost simultaneously with it. Rarely does the pain radiate elsewhere than to the ear or its environs and to the affected side of the throat. It seems probable that Jacobson's nerve is responsible for this aspect of the pain, but as there is no external sensory supply by the glossopharyngeal nerve, pain to the mandible and outer ear must be looked on as referred. At times, as in two of Doyle's cases, in one of Adson's and in one of Harris', the ear was actually tender to touch. In the latter two instances, touching or washing the ear would precipitate the characteristic attacks. Although the method par excellence of starting attacks of glossopharyngeal neuralgia is to drink hot or cold liquids—cold is more effective than hot—the attacks are also induced in many other ways. Other recognized causes are swallowing (solid foods seem to be less effective than liquids), talking, yawning, coughing, shouting, sneezing, touching the ear, suddenly turning the head, and in one instance touching the angle of the mandible, often the attacks seem to occur spontaneously. A trigger zone was present in both of the cases reported (the base of the tongue, near the tonsil), in one of Adson's cases (pharyngeal wall) and in Goodyear's case (tonsillar pillar). Harris remarked on the absence of a "trigger zone" in cases of glossopharyngeal neuralgia, and considered its absence to be almost the only essential difference between glossopharyngeal neuralgia and trigeminal neuralgia, the four cases in which there were trigger zones have appeared since the publication of his book.

Like trigeminal neuralgia glossopharyngeal neuralgia usually appears in the later half of life and usually after the age of 50. Whether significant or not one observation stands out strikingly in this early series, there are only three cases (10 per cent) in women.

I have placed in the same group the cases in which the glossopharyngeal neuralgia was caused by a tumor and those in which it has been considered essential or idiopathic. As a matter of fact, the only reason for having assumed that the condition is idiopathic was the analogy of the features of the pain with those in trigeminal neuralgia. Necropsy was performed only in Weisenburg's case, and an intracranial exposure of the ninth nerve has been made only in my two cases. From the latter cases alone, positive objective proof is furnished of the essential nature of glossopharyngeal neuralgia. As a matter of fact, the proportion of tumors that have been demonstrated is high, compared with their incidence in trigeminal neuralgia. Three of the series of patients are known to have had tumors. Weisenburg's patient with cerebellopontile tumor and two of Harris' patients who had carcinoma of the tonsil. It seems probable that tumors were present in two more instances. One of Harris' patients lost 22 pounds (10 Kg) in weight in two months, indicating a serious wasting underlying cause. Another victim had convulsions induced by the pain, in fact, a cerebral exploration had been made for a tumor of the brain, though with negative results. This patient died a year later, presumably from the intracranial lesion (tumor?). There is, therefore, a known incidence of 15 per cent of tumors in this group and a probable incidence of at least 25 per cent. Weisenburg's case, taken in conjunction with the well known slow, insidious growth of tumors in the cerebellopontile angle, as well as the frequently obscure malignant lesions of the tonsil and nasopharynx, should make one always alert to the possibility that an underlying tumor may be the cause instead of an idiopathic neuralgia. Moreover, a careful survey of the histories in the cases here assembled seems to indicate no discernible difference in the character or location of the pain or its provoking influences, whether there is an underlying tumor or not. One additional great advantage of the intracranial operation for glossopharyngeal neuralgia is that automatically any intracranial lesion is discovered and may be eliminated. If a tumor is causing the condition, no treatment is, of course, rational which does not deal with the removal of the tumor if that is possible.

The diagnosis of essential glossopharyngeal neuralgia is made solely from the history and from observation of the attacks. In many of the cases from the literature a diagnosis of trigeminal neuralgia was made, but this was before the glossopharyngeal neuralgia was recognized. The pain of glossopharyngeal neuralgia was so characteristically located in the region of the ninth nerve that in none of the cases collected here should there be any doubt of the diagnosis. One might possibly think of trigeminal neuralgia when the ear is tender and when touching the ear incites attacks, but even then the pain is mainly induced by stimuli in the back of the mouth, and the pain is always in this region.

Neuralgia of the seventh nerve (geniculate ganglion) has been described by Hunt as accompanied by pains largely localized in the ear.

Geniculate herpes is a well recognized condition, but geniculate neuralgia is none too securely established, at least it remains to be proved that a ticlike neuralgia of the seventh nerve occurs without more spasms. A tic of the facial nerve, described by Cushing as "tic conouloif," is characterized by spasms of the facial muscles, and cannot be confused with glossopharyngeal neuralgia.

GLOSSOPHARYNGEAL NERVE SUPPLY

Isolated loss of function of the glossopharyngeal nerve apparently has not been known. Pope,⁹ in describing a case of thrombosis of the vertebral artery pressing on the glossopharyngeal nerve, quotes Gowers as saying "There is no recorded case in which the roots of the glossopharyngeal nerve alone have been diseased." Cassirer,¹⁰ writing in Oppenheim's *Lehrbuch* makes a similar statement. Cases of tumor or traumatic injuries to the nerves at the base of the skull have paralyzed the glossopharyngeal nerve, but this paralysis has never been purely and solely of the glossopharyngeal nerve. Indeed, Pope's case seems more probably an aneurysm and not a thrombosis, for there was a fusiform mass. In addition to the incomplete injury to the glossopharyngeal nerve, there was partial facial paralysis and some disturbance of the trigeminus, both subjective and objective, moreover, it is difficult to understand how the vagus, which is in such close proximity, could have been spared. It is almost inconceivable that any neoplasm could be so small and so isolated as to cause a pure glossopharyngeal paralysis, and it is equally incredible that any effect of trauma could induce an isolated paralysis of this nerve. Vernet's conclusions on glossopharyngeal function, as noted, which have received much more consideration than they deserve, have been derived from observations of tumors, inflammations and fractures affecting all of these structures in the jugular foramen. From such a source it is impossible to separate disturbances of the ninth and tenth nerves, which are so intimately related over such a long distance. The only possible way to cause pure glossopharyngeal destruction and, therefore, to test the function of this nerve is by intracranial section at operation. Section of the nerve in the neck has always been accompanied by injuries of the vagus and usually of the sympathetic nerve. The entire nerve can never be sectioned or avulsed in the neck for branches—notably Jacobson's nerve—cannot be reached. The two

9 Pope F M. Thrombosis of Vertebral Artery Pressing on Glossopharyngeal Nerve, Unilateral Loss of Taste at Back of Tongue. *Brit M J* 2:1148, 1959.

10 Cassirer. Die Lähmung des N. Glossopharyngeus in Oppenheim, *Lehrbuch der Nervenkrankheiten* 1923 vol 1 p 775.

Table of Cases of Glossopharyngeal Neuralgia Assembled from the Literature

Author and Year	Age and Sex	Duration of Pain	Nature of Pain	Location of Pain	What Induces Pain	Duration of Paroxysm	Pain in Ear	Tender-ness of Ear	Trigger Zone	Pain Unilateral	Pain Has Intermission	Cause of Pain	Treatment
Walsburch 1910	57 ♂		Sharp shooting, dry burning, feeling in throat	Root of tongue	Eating, drinking		+		+	+		Tumor of cerebello pontile angle	Gasserian ganglion
Skard and Robbman 1920	Young soldier	Several years	In, severe paroxysm	Pharyngeal wall	Swallowing, talking, chewing					+	+	None	Peripheral section of ninth, pharyngeal branches of tenth, and sympathetic nerves
Skard and Robbman 1920	Young soldier	Several years	Severe paroxysm	Pharyngeal wall	Swallowing, talking, chewing					+	+	None	Peripheral section of ninth, pharyngeal branches of tenth, and sympathetic nerves
Skard and Robbman 1920	51 ♀		Severe paroxysm	Pharyngeal wall	Swallowing, talking, chewing					+	+	None	Peripheral section of ninth, pharyngeal branches of tenth, and sympathetic nerves
Doyle 1923	63 ♂	20 yr	Severe paroxysm	First in ear, later in tonsillar region	Eating, drinking, talking, yawning		+	+	of auricle	+	+	None	First gasserian, later peripheral section of ninth and tenth nerves
Doyle 1923	42 ♂	3 wk	Severe paroxysm	First in ear, later in throat	Talking, swallowing, spontaneous	20 to 40 seconds	+	+	over trigus after paroxysms	+	+	None	Injection in third branch of fifth and auricular temporal nerve,
Doyle 1923	57 ♀	1 yr	Paroxysms, feeling of choking	Side of pharynx	Drinking	1 to 2 seconds				+	+	None	None
Doyle 1923	61 ♂	9 yr	Intermittent paroxysms	Side of pharynx	Movements of head, talking, swallowing, fright	2 to 50 seconds	+		None	+	+	None	None
Adson 1924	61 ♂	9 yr	Severe paroxysms	Lobule ear and pharynx	Movements of head, swallowing, talking, spontaneous		+	+	lobule Excessive, auricle	+	+	None	Attempted peripheral avulsion of ninth nerve, but nerve later found intact, vagus injured
Adson 1924	42 ♂	1 yr	Severe stabbing pains	Glossil and ear	Drinking, washing ear		+	+	+	+	+	None	Avulsion of ninth nerve, vagus injured

Ad on	Sex	Age	Amfelle's signs	Pharyngeal muscles	Irritation	Drinking, eating, talking, pressure on maxilla	Few seconds to few minutes	None	+	longest 6 mos	None	Avulsion of ninth and part of tenth nerves
Harris 102	♂	17 yr	Severe pyrexias	Left side of throat	Irritation	Swallowing	+	None	+	+	None	
Harris 125	♀	12 yr	Severe pyrexias	Root of tongue	Irritation and back of jaw	Swallowing, eating, yawning	+	Conchoid intensely tender to touch	+	+	None	
Harris 136	♂	6 mo	Severe pyrexias	Throat	Irritation back and neck	Swallowing and touching	+	Touching ear started attacks	+	+	None	
Harris 146	♂	6 yr	Severe pyrexias	Tonsil	Irritation	Yawning but not swallowing	+	27 seconds	+	longest 1 year	None, but had convulsions and died 2 years later (brain tumor?)	Injection in mandibular nerve not successful
Harris 149	♂	1 yr	Pain on swallowing	Tonsillar region	Irritation	Swallowing, hot drinks peculiarly	+	None	+	longest 1 year	Cured	Local removal of ependymoma
Harris 151	♂	1 yr	Severe pyrexias	Side of throat	Irritation	Swallowing, hot drinks peculiarly	+	None	+	longest 1 year	Cured	Local removal of ependymoma
Condon 157	♀	1 yr	Severe pyrexias	Throat and tonsil	Anterior to ear	Swallowing, not chewing	+	None	+	+	Possibly None	
Purdy 158	♀	1 yr	Severe pyrexias	Back of tongue and tonsil	Irritation, back as if pushed out	Swallowing, not chewing	+	None	+	+	None	
Purdy 159	♀	1 yr	Severe pyrexias	Back of tongue and tonsil	Irritation, back as if pushed out	Swallowing, not chewing	+	None	+	+	None	
Purdy 160	♀	1 yr	Severe pyrexias	Back of tongue and tonsil	Irritation, back as if pushed out	Swallowing, not chewing	+	None	+	+	None	
Purdy 161	♀	1 yr	Severe pyrexias	Back of tongue and tonsil	Irritation, back as if pushed out	Swallowing, not chewing	+	None	+	+	None	
Purdy 162	♀	1 yr	Severe pyrexias	Back of tongue and tonsil	Irritation, back as if pushed out	Swallowing, not chewing	+	None	+	+	None	
Purdy 163	♀	1 yr	Severe pyrexias	Back of tongue and tonsil	Irritation, back as if pushed out	Swallowing, not chewing	+	None	+	+	None	
Purdy 164	♀	1 yr	Severe pyrexias	Back of tongue and tonsil	Irritation, back as if pushed out	Swallowing, not chewing	+	None	+	+	None	
Purdy 165	♀	1 yr	Severe pyrexias	Back of tongue and tonsil	Irritation, back as if pushed out	Swallowing, not chewing	+	None	+	+	None	
Purdy 166	♀	1 yr	Severe pyrexias	Back of tongue and tonsil	Irritation, back as if pushed out	Swallowing, not chewing	+	None	+	+	None	
Purdy 167	♀	1 yr	Severe pyrexias	Back of tongue and tonsil	Irritation, back as if pushed out	Swallowing, not chewing	+	None	+	+	None	
Purdy 168	♀	1 yr	Severe pyrexias	Back of tongue and tonsil	Irritation, back as if pushed out	Swallowing, not chewing	+	None	+	+	None	
Purdy 169	♀	1 yr	Severe pyrexias	Back of tongue and tonsil	Irritation, back as if pushed out	Swallowing, not chewing	+	None	+	+	None	
Purdy 170	♀	1 yr	Severe pyrexias	Back of tongue and tonsil	Irritation, back as if pushed out	Swallowing, not chewing	+	None	+	+	None	
Purdy 171	♀	1 yr	Severe pyrexias	Back of tongue and tonsil	Irritation, back as if pushed out	Swallowing, not chewing	+	None	+	+	None	
Purdy 172	♀	1 yr	Severe pyrexias	Back of tongue and tonsil	Irritation, back as if pushed out	Swallowing, not chewing	+	None	+	+	None	
Purdy 173	♀	1 yr	Severe pyrexias	Back of tongue and tonsil	Irritation, back as if pushed out	Swallowing, not chewing	+	None	+	+	None	
Purdy 174	♀	1 yr	Severe pyrexias	Back of tongue and tonsil	Irritation, back as if pushed out	Swallowing, not chewing	+	None	+	+	None	
Purdy 175	♀	1 yr	Severe pyrexias	Back of tongue and tonsil	Irritation, back as if pushed out	Swallowing, not chewing	+	None	+	+	None	
Purdy 176	♀	1 yr	Severe pyrexias	Back of tongue and tonsil	Irritation, back as if pushed out	Swallowing, not chewing	+	None	+	+	None	
Purdy 177	♀	1 yr	Severe pyrexias	Back of tongue and tonsil	Irritation, back as if pushed out	Swallowing, not chewing	+	None	+	+	None	
Purdy 178	♀	1 yr	Severe pyrexias	Back of tongue and tonsil	Irritation, back as if pushed out	Swallowing, not chewing	+	None	+	+	None	
Purdy 179	♀	1 yr	Severe pyrexias	Back of tongue and tonsil	Irritation, back as if pushed out	Swallowing, not chewing	+	None	+	+	None	
Purdy 180	♀	1 yr	Severe pyrexias	Back of tongue and tonsil	Irritation, back as if pushed out	Swallowing, not chewing	+	None	+	+	None	
Purdy 181	♀	1 yr	Severe pyrexias	Back of tongue and tonsil	Irritation, back as if pushed out	Swallowing, not chewing	+	None	+	+	None	
Purdy 182	♀	1 yr	Severe pyrexias	Back of tongue and tonsil	Irritation, back as if pushed out	Swallowing, not chewing	+	None	+	+	None	
Purdy 183	♀	1 yr	Severe pyrexias	Back of tongue and tonsil	Irritation, back as if pushed out	Swallowing, not chewing	+	None	+	+	None	
Purdy 184	♀	1 yr	Severe pyrexias	Back of tongue and tonsil	Irritation, back as if pushed out	Swallowing, not chewing	+	None	+	+	None	
Purdy 185	♀	1 yr	Severe pyrexias	Back of tongue and tonsil	Irritation, back as if pushed out	Swallowing, not chewing	+	None	+	+	None	
Purdy 186	♀	1 yr	Severe pyrexias	Back of tongue and tonsil	Irritation, back as if pushed out	Swallowing, not chewing	+	None	+	+	None	
Purdy 187	♀	1 yr	Severe pyrexias	Back of tongue and tonsil	Irritation, back as if pushed out	Swallowing, not chewing	+	None	+	+	None	
Purdy 188	♀	1 yr	Severe pyrexias	Back of tongue and tonsil	Irritation, back as if pushed out	Swallowing, not chewing	+	None	+	+	None	
Purdy 189	♀	1 yr	Severe pyrexias	Back of tongue and tonsil	Irritation, back as if pushed out	Swallowing, not chewing	+	None	+	+	None	
Purdy 190	♀	1 yr	Severe pyrexias	Back of tongue and tonsil	Irritation, back as if pushed out	Swallowing, not chewing	+	None	+	+	None	
Purdy 191	♀	1 yr	Severe pyrexias	Back of tongue and tonsil	Irritation, back as if pushed out	Swallowing, not chewing	+	None	+	+	None	
Purdy 192	♀	1 yr	Severe pyrexias	Back of tongue and tonsil	Irritation, back as if pushed out	Swallowing, not chewing	+	None	+	+	None	
Purdy 193	♀	1 yr	Severe pyrexias	Back of tongue and tonsil	Irritation, back as if pushed out	Swallowing, not chewing	+	None	+	+	None	
Purdy 194	♀	1 yr	Severe pyrexias	Back of tongue and tonsil	Irritation, back as if pushed out	Swallowing, not chewing	+	None	+	+	None	
Purdy 195	♀	1 yr	Severe pyrexias	Back of tongue and tonsil	Irritation, back as if pushed out	Swallowing, not chewing	+	None	+	+	None	
Purdy 196	♀	1 yr	Severe pyrexias	Back of tongue and tonsil	Irritation, back as if pushed out	Swallowing, not chewing	+	None	+	+	None	
Purdy 197	♀	1 yr	Severe pyrexias	Back of tongue and tonsil	Irritation, back as if pushed out	Swallowing, not chewing	+	None	+	+	None	
Purdy 198	♀	1 yr	Severe pyrexias	Back of tongue and tonsil	Irritation, back as if pushed out	Swallowing, not chewing	+	None	+	+	None	
Purdy 199	♀	1 yr	Severe pyrexias	Back of tongue and tonsil	Irritation, back as if pushed out	Swallowing, not chewing	+	None	+	+	None	
Purdy 200	♀	1 yr	Severe pyrexias	Back of tongue and tonsil	Irritation, back as if pushed out	Swallowing, not chewing	+	None	+	+	None	

cases here reported are presented as pure isolated lesions of the glossopharyngeal nerve, there were no other involvements of the cranial nerves. The after-effects of division of the glossopharyngeal nerve intracranially were almost the same in both cases.

Motor Changes—Symptomatically, there was absolutely no subjective or objective motor disturbance in either instance. Swallowing was unaffected. The constrictors of the pharynx were unimpaired. The soft palate moved normally and equally on the two sides. Most text-books of anatomy agree that the stylopharyngeus muscle is the only muscle supplied by the glossopharyngeal nerve. I do not know of any test that will demonstrate its loss of function, apparently its absence (if the nerve is affected) is not noticeable to the patient. These cases, I believe, effectually contradict the claims of Vernet that the important middle constrictor of the pharynx is supplied by this nerve, its nerve supply is from the vagus.

Alterations of Taste—The nerve supply of taste will shortly be the subject of a more detailed study in conjunction with Dr. Dean Lewis. For this reason, only cursory mention will be made here of the part played by the ninth nerve in the supply of taste to the tongue as a whole.

In both of the cases reported there was complete loss of taste in the posterior third of the tongue. This confirms the usual conception of the nerve supply of taste for this part of the tongue. It opposes the rather unusual view long taught by Gowers and others that the trigeminal nerve supplies taste to the whole tongue. In one of the cases reported here, no change occurred in the perception of taste in the anterior two thirds of the tongue. In the other case there was a slight, but definite, alteration to the degree that on the normal side, sweet, sour, bitter and acid were all recognized more quickly (a few seconds) and registered with greater intensity than on the side with the cut glossopharyngeal nerve, but all tests for taste were accurately registered on the affected side (anterior two-thirds). The interpretation of these minor alterations of taste in one case and none in the other will be discussed in the forthcoming paper. At least, it is evident that the ninth nerve supplies taste for the posterior third of the tongue, but does not supply taste to the whole tongue, a view long held by Luciani and by his followers even at present.

Sensory Changes—The results in both cases are best shown in the accompanying sketches. For the examinations of the sensory loss in the pharynx and nasopharynx and the base of the tongue I am indebted to Dr. S. J. Crowe. The only differences noted in the two cases were that in one patient sensation was perceived in the eustachian tube for a few millimeters below the pharyngeal orifice, in the other there was no sensation for a distance of about 2.5 cm. In one patient the sensory deadline exactly bisected the uvula, in the other almost the

entire uvula was anesthetic. In both patients, a cap of sensation remained at the vault of the nasopharynx, doubtless being supplied by the trigeminal nerve. The remainder of the pharynx, anterior, posterior and lateral, down to the epiglottis (including the posterior aspect) the vellicula and the pyriform sinus, was anesthetic. Anteriorly and posteriorly, the line of anesthesia ended sharply at the midline. The soft palate is supplied by the glossopharyngeal nerve only in a narrow rim on its oral surface and over a greater extent on its nasal surface. The tonsil and eustachian orifice were insensitive in both cases. The epiglottis was anesthetic on its posterior aspect, the line of demarcation of the area with the normal sensation of the anterior surface from that supplied by the vagus is a sharp line along the rim of the epiglottis. The precise line of demarcation between the area of normal and of lost sensation was difficult to determine in two places—above at the vault of the nasopharynx and below at the beginning of the esophagus. These two narrow zones are therefore shown in dots in contrast to the cross-hatch which denotes the absolute loss of sensation. The anterior wall of the sphenoid and the posterior end of both the middle and inferior turbinates were sensitive. There was no area of anesthesia in the nasal cavity. It could not be determined whether there was any loss of sensation along the posterior border of the vomer.

Secretory and Sympathetic Nerves—No disturbance of salivary secretion could be detected after the glossopharyngeal nerves had been sectioned.

I am aware that the small superficial petrosal nerve is a continuation of Jacobson's nerve through the tympanic plexus. It has received much attention as an important link in the chain of certain theories of taste, it has been supposed also to carry sensation to the nasal cavity even to the pharynx. I have not been able to adduce evidence of either function.

SUMMARY AND CONCLUSIONS

1 Glossopharyngeal neuralgia is a type of *tic douloureux* exactly like trigeminal neuralgia. Its clinical picture is so characteristic and the history of the attacks so vivid that the diagnosis is easy and unmistakable.

2 Two cases are reported and appended to eighteen others which have been assembled from the literature. The clinical features of this condition are analyzed and tabulated.

3 The treatment of glossopharyngeal neuralgia is purely surgical. An operation by which the ninth nerve is sectioned intracranially was carried out in both cases. The superiority of this operation over section of the glossopharyngeal nerve in the neck is due to the fact that other nerves are not injured and the nerve is cut above the ganglion.

thereby precluding return of the malady. The operation is practically without danger to life and leaves no subjective or objective disturbance in its wake.

4. These isolated glossopharyngeal lesions afford an excellent opportunity to study the function—sensory, motor and gustatory—of this nerve. It is probable that these cases are the only instances of pure, unmixed and total loss of function of the ninth cranial nerve.

EXPERIMENTAL OBSERVATIONS ON THE GROWTH OF LONG BONES

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AND

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Our attention was attracted to the question of growth of bone by Haas' article in the *ARCHIVES OF SURGERY*,¹ in which he reviewed fully the large amount of experimental work which had previously been done. It is of interest to note that the first work of this type was done by Duhamel in 1739, and that John Hunter made some careful experiments on growth of bone ninety years ago. While his results—still preserved in the Hunterian Museum—do not show any longitudinal increase in the shaft of bone in pigs and fowls, he concluded nevertheless that some growth can occur. Ollier,² a young Frenchman from Lyons, coming to Paris in 1857, attracted by that genius of medical research, Claude Bernard, plunged into this fascinating problem in the laboratory of Chaveau. After a series of experiments with periosteum, he became completely convinced of its osteogenic properties. He also noted that irritation of the shaft of a bone could cause increase in the rate of growth of the epiphyses, and that it might even cause an overgrowth of as much as one-fifteenth of the total length of the bone. He repeated Duhamel's experiments to make certain in his own mind that longitudinal growth took place only at the epiphyseal lines.³ He found slight separation of markers placed in ends of the shafts of young fowls, but not enough to change Duhamel's rule of nonelongation.

In spite of this experimental evidence clinical observers have felt that, although most of the growth took place in the epiphyses, still a small amount could occur in the shaft. Truesdell,⁴ Speed,⁵ David,⁶ and

1 Haas, S. L. Interstitial Growth in Growing Long Bones, *Arch. Surg.* **12** 887 (April) 1926.

2 Keith, Arthur. Bone Growth and Bone Repair. *Brit. J. Surg.* **6** 160 (1919).

3 Ollier, Louis. *Traité expérimental et clinique de la régénération des os et de la production artificielle du tissu osseux*. Paris, 1867.

4 Truesdell, E. D. Inequality of the Lower Extremities Following Fracture of the Shaft of the Femur in Children. *Ann. Surg.* **74** 498 (Oct.) 1921.

5 Speed, K. Longitudinal Overgrowth of Long Bones. *Surg. Gynec. Obst.* **36** 787 (June) 1923.

6 David, A. C. Overgrowth Following Fracture. *Arch. Surg.* **9** 438 (Sept.) 1924.

Harbin⁷ have all reported instances of the overgrowth of bone following fracture or irritation of the shaft. Of all these cases overgrowth of the epiphyses could be excluded in only one, which was reported by Speed. The patient was 45 years old, so that compensatory epiphyseal growth was out of the question. Increase in length of bone in tertiary syphilis is not an uncommon observation, and it seems to be fairly characteristic of Paget's disease. While enormous increase has frequently been noted in acromegaly, one can fairly question how frequently actual lengthening occurs in the shaft of the long bones after the epiphyses have closed. There is no doubt, however, about the increase in the length of the ribs and the mandible. McEwen's⁸ well known case of resection of the humerus for osteomyelitis, with subsequent transplantation of bone is an oft-cited example of growth of longitudinal bone. The patient, then 3 years old, was operated on in 1878. This is probably the earliest successful bone graft on record. At the time of operation, a graft $4\frac{1}{2}$ inches (11.2 cm) long, taken without periosteum, was inserted into a large defect of the humerus. Thirty years later, the graft measured 6 inches (15.2 cm). The picture, included in his book, "The Growth of Bone," is difficult to interpret and to me not altogether convincing.

Haas, employing essentially the same technic which we shall describe, demonstrated almost incontrovertibly that no longitudinal growth occurs in the shaft of the tibia of the dog or in the metatarsals of the rabbit.

Still a bit skeptical, thinking that perhaps the cancellous bone near the epiphyses, being softer and more readily absorbed, might possess the property of increasing in length, we placed, not two markers near the center of the shaft as has usually been done, but several, 1 cm apart along its entire length, so that any change occurring in the diaphysis might be observed.

EXPERIMENTAL WORK

Seventy-nine experiments in all were performed on young rabbits. Thirty-nine rabbits died of exposure or epidemic, leaving forty from which deductions might be drawn.

Method—Under ether anesthesia, employing careful aseptic technic, the lateral surface of the femur was exposed throughout its entire length. This was done by making an incision parallel to the femur on the lateral surface of the thigh. After the skin and fascia lata were divided, the vastus lateralis and intermedius were retracted anteriorly and the biceps femoris posteriorly. Then, after the

⁷ Harbin, M. Non-Suppurative Osteomyelitis, *J. Bone & Joint Surg.* 8:401 (April) 1926.

⁸ McEwen, W. The Growth of Bone, Glasgow, Maclehose Jackson & Co. 1912.

lower margin of the insertion of the gluteal muscles had been cut a metal rule was placed parallel to the femur, and marks 1 cm apart were made on the bone with a knife. A small notch was made over each mark and in these notches holes were drilled, care being taken not to go completely through the cortex. The drill used was slightly smaller than the shot inserted so that it was possible to inlay the shot snugly into the holes. The shot rarely entered the canal of the marrow. The attachment of the gluteal muscles, the fascia lata and the skin were approximated with catgut, and a dressing of collodion was applied. There was only slight temporary impairment in the function of the leg after operation. Roentgenograms were usually made the following day. All films were made with the leg of the animal held firmly against the plate and with a uniform target distance of 24 inches (60.9 cm). The superimposability of the films attests to the accuracy of the method.

Five series of experiments were performed as follows:

Series 1—Only three or four shot were inserted. An attempt to close the lower epiphyses was made by removing from 1 to 2 cm of the distal periosteum leaving the articular cartilage adjacent to the outer margin of the epiphyseal plate intact.

Series 2—From five to seven shot were inserted in the femur 1 cm apart, care being taken not to disturb the periosteum or the blood supply to the epiphyseal plate. The end shot were placed close to the epiphyseal plates, and in rabbit 30 the lower shot was placed directly in the cartilage plate.

Series 3—Shot were inserted in a manner similar to that used in the second series, except that an attempt was made to close the epiphyses by removing from 1 to 2 cm of the distal periosteum, together with that part of the articular cartilage directly over the epiphyseal plate. Several parallel holes were drilled through the epiphyseal plate with a fine drill.

Series 4—A procedure similar to that of series 3 was followed with the exception that holes were not drilled in the epiphyseal cartilage plate.

Series 5—Parallel holes were drilled in the epiphyseal plate but no attempt was made to destroy its blood supply by removing the adjacent periosteum or articular cartilage.

It is evident from the following experiments that normally no growth of the diaphyses occurs in rabbits except at the epiphyseal cartilage plate and that if the shot is introduced carefully into the epiphyseal plate there is little or no retardation of growth (plate 30).

For the sake of brevity only a few protocols are given and a few typical plates are shown.

Series 1, Rabbit 15—The epiphyses were not completely closed. Three shot were inserted into the shaft of the left femur about 1 cm apart. An attempt to close the epiphyses was made by destroying from 1 to 2 cm of the distal periosteum leaving the adjacent articular cartilage intact. Roentgenograms were made

and fifty-eight days after operation show no separation of the shot, but show an increase in the length of the diaphysis occurring proximal and distal to the shot

Series 2, Rabbit 30—The epiphyses were not closed. Seven shot were inserted in the shaft of the left femur about 1 cm apart. The epiphysis with its blood supply was not disturbed. Roentgenograms taken three, fifty-two and eighty-four days after the operation show no separation of the shot, but show an increase in the length of the diaphysis occurring proximal and distal to the shot.

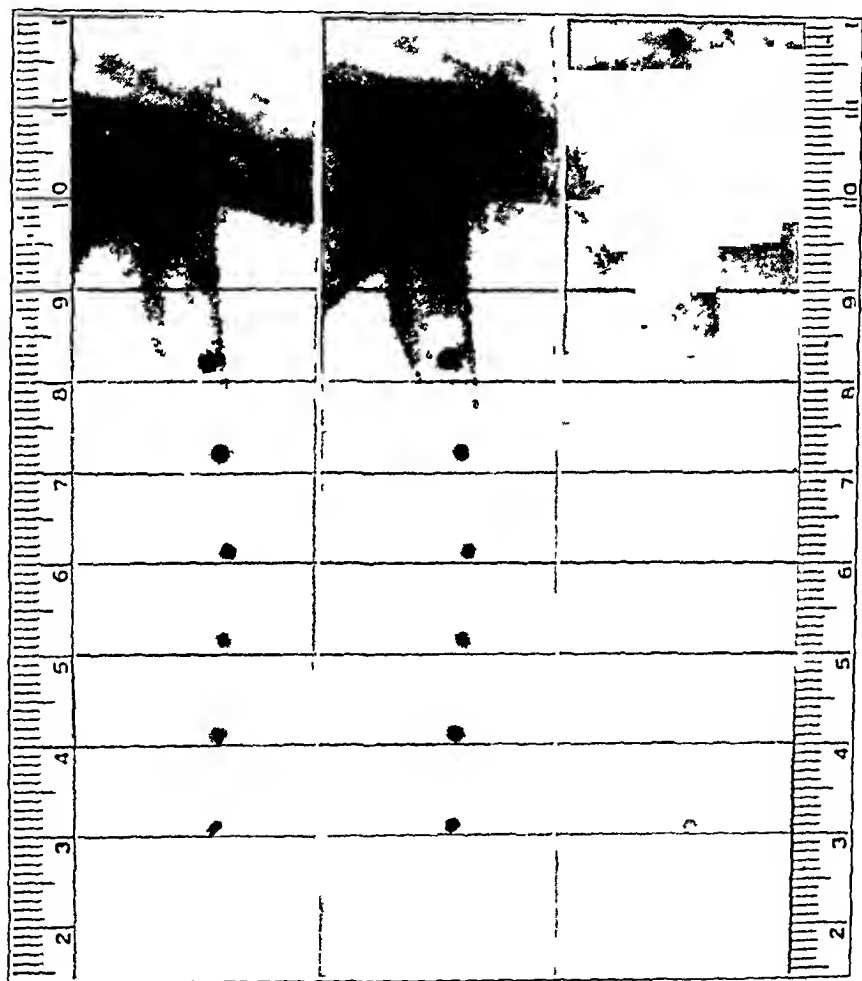


Fig 1—Roentgenograms of rabbit 30 taken three days, fifty-two days and eighty-four days after operation. The marker is in the epiphyseal cartilage plate. The epiphyses were open, and there was no separation of the shot.

It is also evident that when an increased functional demand is made by closure of the epiphyses no compensatory growth in the diaphysis occurs.

Series 3, Rabbit 39—The epiphyses were closed. Six shot were inserted in the shaft of the left femur about 1 cm apart. An attempt to close the epiphyses was made by destroying the periosteum with its blood supply and the articular

cartilage nearest the epiphyseal cartilage plate and by drilling holes parallel to and through the epiphyseal cartilage plate. Roentgenograms taken one forty-seven and seventy-six days after operation show no separation of the shot, but a slight increase in the length of the shaft, occurring at both ends, but to a greater degree at the proximal end.

Closure of the epiphyses was not as readily accomplished in the rabbit as one might suppose. In some of his experimental work on dogs, Dr. Phemister had found that scraping the periosteum and peeling

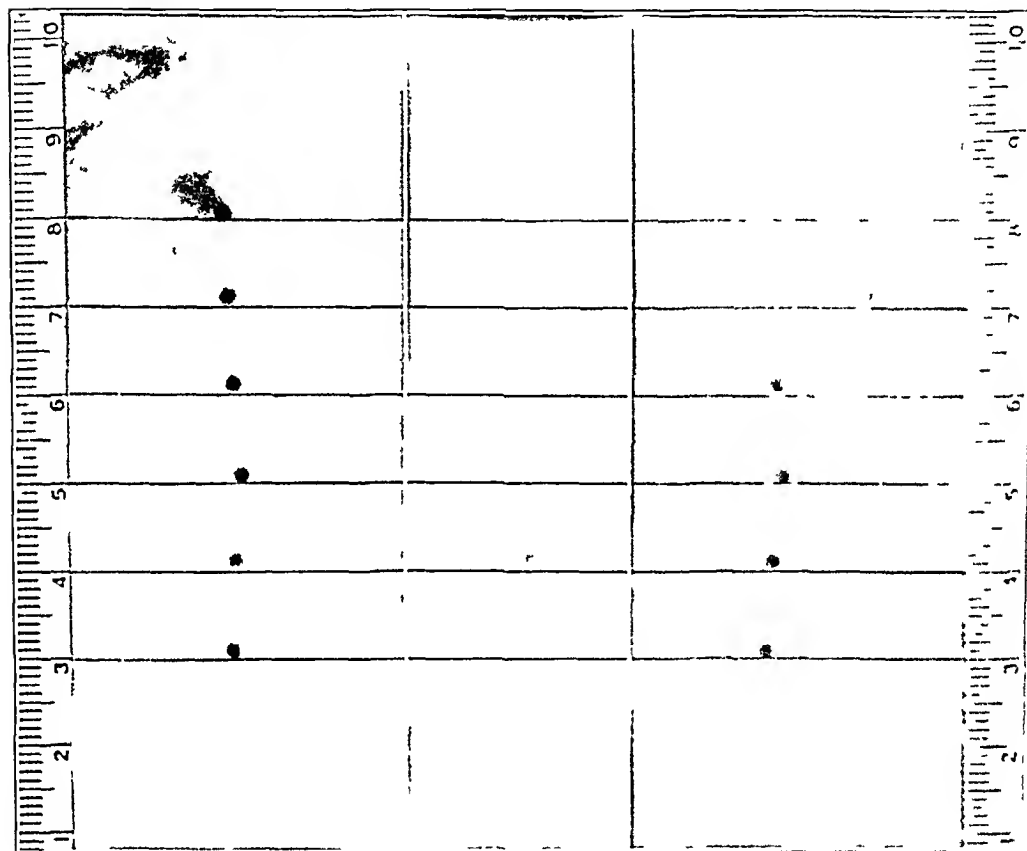


Fig. 2—Roentgenograms of rabbit 39 taken one fifty-two and eighty-four days after operation. The epiphyses were closed and there was no separation of the shot.

the articular cartilage from the epiphyses was sufficient to cause cessation of growth. Haas,⁹ however, working with rabbits, found that this procedure would hasten but not immediately effect closure of the epiphyses. In series 1 removal of the periosteum alone was performed with little success. In series 4 both the periosteum and the articular

⁹ Haas, S. L. The Relation of the Blood Supply to the Growth of Bone. *Am. J. Orth. Surg.* **15**: 15 and 305, 1917.

cartilage nearest the epiphyseal plate were removed, with evident retardation of growth, but in none was there immediate cessation of growth

Series 4, Rabbit 60—The epiphyses were closed Six shot were inserted in the shaft of the left femur about 1 cm apart An attempt to close the epiphyses was made by destroying the periosteum with its blood supply and the articular cartilage nearest the epiphyseal plate Roentgenograms taken three days and forty-four days after operation showed no separation of the shot, but a definite increase in the length of the diaphyses occurring both distal and proximal to the shot

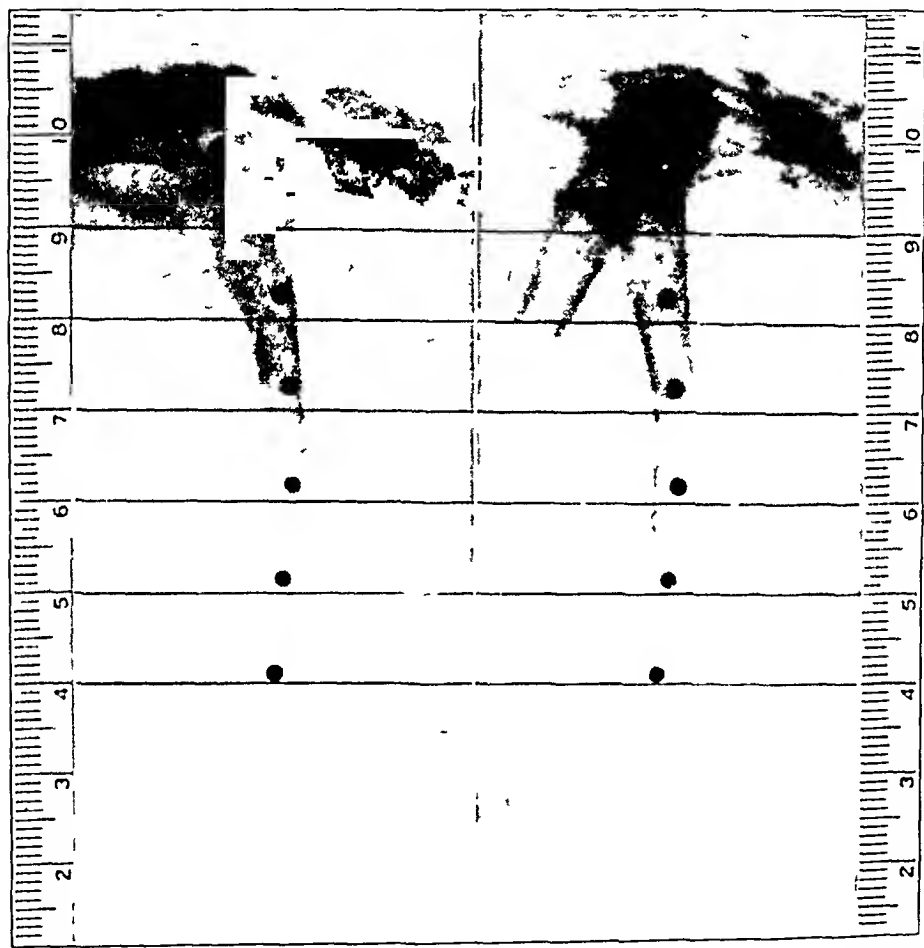


Fig 3—Roentgenograms of rabbit 60 taken three and forty-four days after operation The epiphyses were open, and there was no separation of shot

In series 5, an attempt was made to destroy the cartilage plate by drilling holes parallel to and through the plate From five to seven holes drilled in this manner were sufficient in most cases to close the epiphyses, provided that the holes were drilled near the distal sides of the plate This procedure seemed to be just as effective alone as when used together with scraping of the periosteum and articular cartilage as in series 3

Series 5, Rabbit 70—The epiphyses were closed. Six shot were inserted in the shaft of the left femur about 1 cm apart. An attempt to close the epiphyses was made by drilling holes parallel to and through the epiphyseal plate. Roentgenograms taken three and thirty days after operation showed no separation of the shot, but a slight increase in the length of the diaphyses occurring both distal and proximal to the shot.

CONCLUSIONS

From these experiments it seems evident that in rabbits

1 No longitudinal growth occurs in the diaphyses of long bones except at the epiphyseal cartilage plates, either under normal conditions

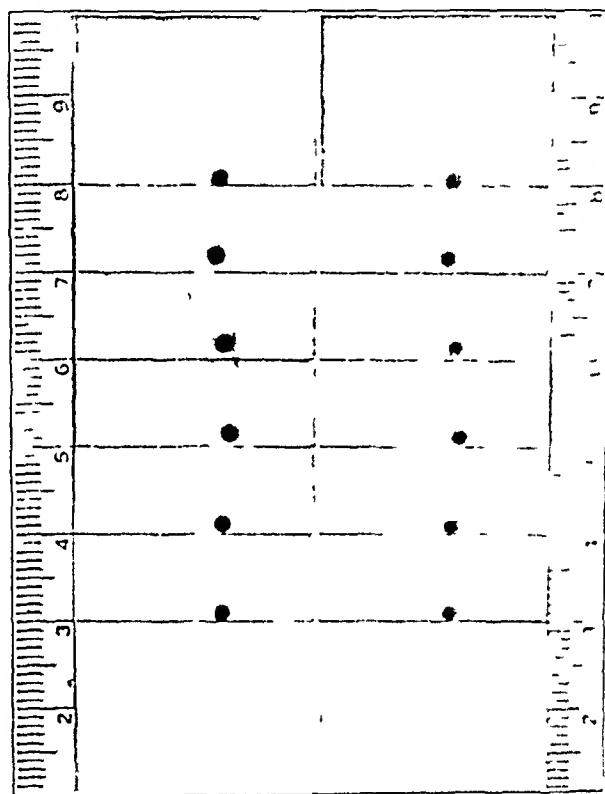


Fig. 4—Roentgenograms of rabbit 70 taken three and thirty days after operation. The epiphyses were closed and there was no separation of the bone.

or when an increased functional demand is made by closing or hastening the closure of the epiphyses.

2 Destruction of the extrinsic blood supply to the epiphyses by removing the adjacent periosteum and articular cartilage is sufficient to close the epiphyses immediately, but will hasten the closure.

3 Immediate closure of the epiphyses can be accomplished by destroying the epiphyseal cartilage plate on the side nearest the

PARAPLEGIA ASSOCIATED WITH CONGENITAL SCOLIOSIS *

REPORT OF A CASE

KENNETH G MCKENZIE, M D
WITH COMMENTS BY CLARENCE L STARR
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History—During December, 1925, a youth, aged 18,¹ was admitted to the Toronto General Hospital. His legs were almost completely paralyzed, and there was a marked curvature of the spine. After a careful study and consideration of the history and roentgenograms it was believed that the spinal curvature was not of tuberculous origin. The case immediately attracted special interest, since no one on the surgical staffs of either the General or the Sick Children's Hospitals could recall having seen a case of paraplegia due to congenital scoliosis.

A case reported by Sachs encouraged us in our opinion that the paralysis was caused directly by the deformity of the spinal canal, and not by some separate pathologic process, such as a tumor.

The patient said that apparently his back was straight until he was 7 or 8 years of age, when his mother first noticed a slight curvature. At the age of 10 or 11, the deformity became obvious. At that time he developed the habit of leaning against any solid object for support, to ease his back, but at no time was there any great amount of pain, although in the mornings his back would ache slightly. He was active and was a good runner and bicycle rider. Two years prior to presentation he ran errands for a butcher, and after carrying the heavy baskets, he noticed that his right side was tired at night. About one year later, a gradual onset of weakness in the right leg was noticed, and he often tripped. A few months later, the other leg became involved, and he was unable to walk a block without getting tired, but he could still ride his bicycle. The weakness of the legs progressed gradually and was most marked in the right leg. Two weeks prior to presentation, it was practically impossible for him to walk, numbness was noticed over the base of the spine and the shin of the right leg, and there was some incontinence of urine.

Examination—An examination of the patient on admission to the hospital showed that both legs were spastic, especially the right, and that they could be raised and lowered slowly. The reflexes at both knees and ankles were markedly exaggerated. There was a marked bilateral ankle clonus and positive Babinski sign. Areas in which sensation to pin-prick was dull were scattered over both legs, and at various points the patient showed inability to differentiate heat from cold.

The patient was put on a Bradford frame with efficient extension of the spine for two months, but despite this, the paraplegia and sensory loss slowly progressed.

Two months after admission an examination showed that there was no voluntary movement of the right thigh, leg, foot or toes. There was slight flexion of the left knee with some movement of the toes. The reflexes were markedly exaggerated at the knee and ankle, with bilateral ankle clonus and positive

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Babinski signs The sensory changes which were present at the time are shown in figure 1. There was incontinence of urine. A lumbar puncture was performed with the Ayer manometer, and the spinal fluid showed an initial pressure of 25 cm of fluid. There was no response on jugular compression. The fluid showed no tinge of yellow, the Pandy test was strongly positive with 1 drop, the Ross-Jones test was also strongly positive. The total protein was not estimated. It was obvious from the examination that the patient had a complete block of the spinal subarachnoid space and that the paraplegia was rapidly progressing.

The motor disturbance was most noticeable in the right leg. Inability to differentiate heat from cold was most marked on the left. Sensation to light touch with wool and a pin scrape was dull on both sides, but was better appre-

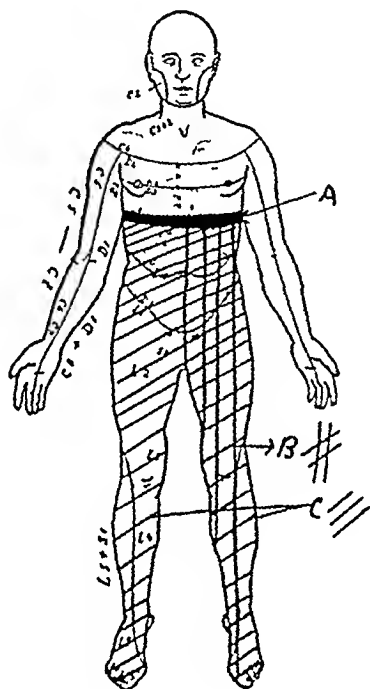


Fig. 1.—Sensory changes present two months after the patient was admitted to the hospital. *A* indicates the band of hyperalgesia. *B* the area in which there was inability to differentiate heat from cold. *C* the area in which sensation to pinprick was dull, it was sharper on the left side. Sensation to light touch dull over both legs but more acute over the left.

erated on the left. These observations suggested that the greatest interference with function was in the right half of the spinal cord.

Iodized oil was injected by the cisternal route and a metal marker placed on the skin. A roentgenogram taken after the patient had been lying on her back fifteen minutes showed that the iodized oil was arrested at the point of maximum curvature and definitely demonstrated the situation of the total block of the subarachnoid space (fig. 2).

Operation and Course.—April 15. Operation was performed on the patient. The marker on the skin enabled one to place the incision. A moderate amount of difficulty was encountered in covering the incision, the left scapula being necessary. When the incision was closed, the

to be filled with a vascular, fatty tissue. On clearing away this fat, it was apparent that the canal was large, with the comparatively small dural sac lying tightly against the bone on the inner side of the curve (fig 3). Two roots were cut, which were tightly stretched in their dural sheaths. The dura was then opened, care being taken to keep the arachnoid intact. The cord immediately bulged out so that the edges of the dura were separated by at least 1 cm (fig 4). There was no apparent subarachnoid space over the cord except in the lower and upper parts of the field, where the cord was covered with a thin layer of fluid, that is, the point of maximum constriction of the cord by the dura was in the center of the field. At this point the vessels on the cord were barely



Fig 2—Exact situation of the block in the subarachnoid space, as shown by a cisternal injection of iodized oil, is indicated by the lower arrow. The skin marker is seen in the upper part of the figure.

apparent, but they were visible above and below. The dura was left open, in fact, there was no other choice. The subarachnoid space over the surface of the cord, at the point of maximum curvature, showed no signs of filling when closure was commenced. There was no evidence of the iodized oil in the subarachnoid space above, but, as the patient was on his face, this would be on the under surface of the cord, and not visible. There was no evidence of inflammatory reaction from the iodized oil, which had been injected two weeks previously. After all bleeding had been carefully controlled, closure of the muscle was made with three layers of interrupted chromic catgut sutures.

It was satisfactory to have been able to preserve the arachnoid intact. Because of this it was felt that a leak of cerebrospinal fluid would be unlikely,

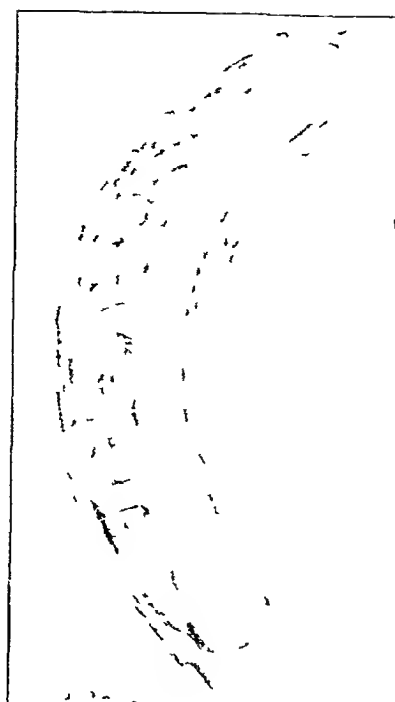


Fig. 3—Marked enlargement of the bony canal on the outer side of the curve. On the inner side of the curve the dura is seen lying tightly against the bone. The dural sac is obviously much smaller at the point of maximum curvature.



Fig. 4—Bulging of the cord after the dura was opened. This gives a more definite impression of the extent of the lesion. After the opened dura the arachnoid was kept in place.

and that adhesions would not form between the cord and the overlying muscle. The chief concern was lest the dura had not been opened over a sufficiently wide area to relieve pressure on the cord completely.

April 14 The patient was able to move his left ankle, whereas before operation he could barely move his big toe.

April 15 The patient moved both ankles rather freely and felt pinching over both thighs. There was control of the bladder.

Progress continued to be rapid. The patient was fitted with a spinal jacket, and was allowed to walk in six weeks. A roentgenogram taken at this time (fig 5), showed the iodized oil at the bottom of the canal.



Fig 5—Six weeks after the operation. Most of the iodized oil is at the bottom of the spinal canal. The two silver clips in the upper part of the figure were left in to mark the point at which the cord appeared to be most constricted.

The patient was examined by the surgical staff of the Toronto General Hospital, Jan 15, 1927, nine months after his operation. There was excellent power in both legs so that he was able to stand with ease on his tiptoes, and readily climbed on to a table. There were no subjective or objective sensory changes. The function of the bladder apparently was normal. The reflexes were still exaggerated at the knees, but he did not have ankle clonus, and response to plantar stimulation was normal.

COMMENT

BY CLARENCE L. STARR

The case presented by Dr. McKenzie has many points of interest, not least of which is the salvage of this patient from the derelict group. I believe that he would never have recovered by any other than operative means. His recovery is complete so far as his nervous system is concerned, and since the deformity appears fixed it is unlikely that the paraplegia will recur.

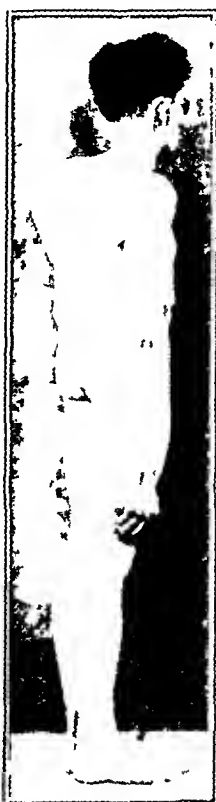


Fig. 6—A photograph taken on discharge from hospital showing the deformity of the back.

The diagnosis is the important factor in all of these cases of paraplegia.

In Pott's disease one frequently sees paraplegia occurring in an early stage of the disease. This is never due to bony narrowing of the canal, but to thickening of the meninges owing to the extension of the infection from the bony focus. Occasionally it may be due to the pressure of an abscess or, more rarely, to a portion of bony sequestrum protruding into the vertebral body or pedicle.

In all autopsy specimens ample space is shown although the cord is shown displaced vertically. In the few cases in which it is found to be true disc disease the spinal cord is displaced laterally.

In childhood or adolescence, extradural fat is found diffusely scattered about the cord, apparently filling up the unoccupied space. Operative measures are for the most part unnecessary in these cases as nearly all patients recover with fixation or traction.

In structural or idiopathic scoliosis, even when the deformity has advanced to an extreme degree, paraplegia must be extremely rare as no cases have come under my observation.

In scoliosis following poliomyelitis, even when the deformity is great, paraplegia must be exceedingly rare as no cases have been seen in our clinic. Elmslie¹ reports one case with high grade deformity at the level of the fifth dorsal segment, due to poliomyelitis contracted at 7 years of age. The scoliosis developed when the patient was 8 years old, a spastic paraplegia commenced at 16 and progressed so that she was unable to walk at 17. She had anesthesia from the xiphoid down. Iodized oil injected into the cisterna magna showed a complete block at the sixth dorsal vertebra. Laminectomy was performed, and the dura was found stretched over the deformity, which was opened and left open. Muscle fascia was closed over the canal. The patient improved, but never to the extent shown in the case reported by Dr. McKenzie. At the end of one year, voluntary movements of the legs were possible, and she was beginning to make an effort to walk. Collier² reports a similar case which he believed was due to poliomyelitis. Scoliosis was noted at 4 years of age. At 14, the legs began to drag, and at 15, she had loss of sphincter control and spastic paraplegia. Sensation was diminished from the seventh dorsal vertebra down. An operation was not performed, but Mr. Collier suggested that decompression was indicated if no improvement was noted after rest and extension.

Five cases of congenital scoliosis with late symptoms of paralysis have been found in the literature, besides the case reported by Dr. McKenzie. Collier² reports one patient with a congenital defect in the upper dorsal vertebrae who first showed signs of weakness at the age of 10. There was progressive weakness with spasticity and exaggerated reflexes, including loss of bladder control. Iodized oil injected into the cisterna magna showed a block at the third dorsal vertebra. Treatment was not instituted.

Kleinberg³ reports a case of congenital scoliosis with marked deformity in a girl, aged 7. At the age of 7 years and 6 months she

1 Elmslie, R. C. Two Cases of Scoliosis with Paraplegia, *Proc. Roy. Soc. Med. Sec. Orth.*, no. 8, 18, 25 (June) 1925.

2 Collier, James. Case of Paraplegia in Scoliosis, *Proc. Roy. Soc. Med., Sec. Neurol.* no. 9, 18, 8 (Feb.) 1925.

3 Kleinberg, S. Structural Scoliosis Complicated by Paralysis of the Lower Limbs. Report of a Case, *J. Bone & Joint Surg.* 5, 104, 1923.

rapidly developed a spastic paraplegia. The patient improved when placed in a recumbent position on a plaster bed and with extension applied. Ultimately she was able to walk freely.

Sachs⁴ reports a case, apparently of congenital scoliosis with paraplegia, in which the patient recovered following operation.

Jaroschy⁵ reports a case from the Biede Clinic of Prague. A patient, who had a severe deformity in the cervical spine in early childhood, rapidly developed paraplegia at the age of 18 and was finally completely bedridden. Roentgenograms showed a wedge-shaped halt vertebra at the fourth dorsal and only eleven ribs were found on the right side. Neurologic examination revealed the usual spastic paraplegia with exaggerated reflexes and sensory disturbance. Laminectomy showed a good deal of epidural fat with apparent stretching of the dura over the prominence. The dura was not closed and the muscles and fascia were closed over the cord. Ten weeks after operation the patient showed marked improvement. He could walk with two sticks; the spastic condition had disappeared, and the reflexes were normal. Sensation was almost normal.

A second case is reported in a girl aged 14 who had deformity at the age of 2, but no signs of weakness developed until seven years later. At the time of examination a roentgenogram showed a congenital defect similar to that in the first case and spastic paraplegia with exaggerated reflexes. There was no sensory or sphincter disturbance. Treatment by extension for three weeks did not cause any change in the condition, and a laminectomy was performed. The dura was not indurated, but it was opened and left open. Seven months after operation the patient was able to get out of bed greatly improved. An examination one year after operation showed that she was able to walk freely. A slight increase in reflexes was the only pathologic symptom.

Riddell⁶ reports two cases, one apparently of congenital scoliosis with paraplegia in which the patient was placed in a recumbent position on a hyperextended frame. At the end of three years the reflexes were much improved but still overactive. Sensory reactions were normal. The second case was apparently one of spinal bifida and the paraplegic symptoms were obviously due to the congenital defect of the cord.

The case presented by Dr. McKenzie is, I believe, one of a congenital defect in the bony spine and is the only one I have seen completely

4. Sachs, Ernest. "An Unusual Case of Paraplegia Associated with Congenital Scoliosis," *Annals of the Royal College of Surgeons in England*, 1925, 10, 100. Also in *Gibbus and a Localized Collection of Fibrous Tissue in the Spinal Column*, 1925, 10, 100. *Joint Surg.*, 7:709, 1925.

5. Jaroschy, W. "Delayed Lesion of Spinal Cord in a Case of Congenital Scoliosis," *Prager Klin. Wochenschr.*, 1925, 47, 152. Also in *Prager Klin. Wochenschr.*, 1925, 47, 152.

6. Riddell, John. "Report on Two Cases of Paraplegia," *British Medical Journal*, 1916, 1, 100. Also in *British Medical Journal*, 1916, 1, 100. (Sept. 9, 1916).

complete paraplegia. The extreme deformity without paralytic onset, the early appearance of deformity and the obvious segmentation of several of the upper dorsal vertebrae point to the congenital origin. Clinical or roentgen-ray signs of abscess were not noted, and evidence of tuberculous disease was not present in the neural canal at operation.

In my opinion, the extradural fat found at operation, as in the case reported by Sachs, was not a factor in the causation of the paraplegia.

The rapid restoration of the form of the cord from the flattened shape to the normal rounded appearance and the commencement of pulsation after the opening of the dura seem to prove conclusively that the cause of the paraplegia was the pressure of the cord against the acute bony angle, by the taut dura.

FATAL PULMONARY EMBOLISM

A STATISTICAL REVIEW

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Records of postmortem examinations at the Mayo Clinic for the last ten years show that pulmonary embolism occurred in 313 cases, in 267 of these, the complication followed operation and in 46, it occurred in nonsurgical cases. In 223 (83.5 per cent) of the 267 cases, emboli were the primary cause of death, and in 44 (16.5 per cent), they were either contributory factors or were so small that they had little or no connection with the patient's death.

One hundred and four of the patients who died from embolism were men and 119, women, their average age was 53.2 years. The average age of 1,000 adult patients operated on consecutively was found to be 42.8 years. Therefore, the average age of the patients dying from embolism was 10.4 years greater than that of the average patient coming to operation. The average height for these patients was 5 feet, 6.5 inches (168.9 cm), and the average weight, 168 pounds (76.2 Kg). The normal weight for persons of this age and height has been estimated at 155 pounds (70.3 Kg), so these patients averaged 13 pounds (5.9 Kg) overweight. The fact that most of them were ill when they came to the clinic and definitely below their usual weight must also be taken into consideration. The average systolic blood pressure was 138 and the average diastolic blood pressure, 82, which is a normal or somewhat subnormal blood pressure for patients of this age. That massive pulmonary embolism may occur in hypertension is shown by the fact that the systolic blood pressure was more than 200 in five cases in the series, the highest pressure encountered being 260.

The operation leading to fatal embolism in this series was extra-abdominal in 43 cases (19.3 per cent) and intra-abdominal in 180 (80.7 per cent). Forty-four per cent of the operations within the abdomen were performed in the upper portion and 51.6 per cent in the lower portion, 3.7 per cent were explorations and 0.5 per cent paracenteses. In this series, therefore, there was no great difference in the number of deaths from pulmonary embolism following operations in the upper and in the lower portion of the abdomen.

A more detailed review of the cases of embolism occurring after intra-abdominal operations (table 1) shows that the most frequent cases following operations on the gallbladder and ducts was 0.7 per cent, on the stomach 0.25 per cent, on the uterus and vagina 0.25 per cent, and on the

cent, on the prostate, 0.46 per cent and on the bladder (cystostomy preliminary to prostatectomy), 1.5 per cent. That the incidence of embolism is higher after cystostomy alone than after prostatectomy is probably accounted for by the fact that the patients undergoing cystostomy were such poor risks that they were not subjected to the one-stage operation.

TABLE 1—*Pulmonary Embolism Following Intra-Abdominal Operations*

Operations on	Total Number of Operations, 1917-1926	Cases of Embolism		Incidence of Embolism	
		Number	Percentage	All Cases, Percentage	Fatal Cases, Percentage
Gallbladder and ducts	11,689	37	17.2	0.31	0.30
Stomach	12,453	38	17.6	0.30	0.25
Uterus and appendages	11,961	51	23.7	0.42	0.33
Bladder					
Cystostomy for hypertrophy of prostate	1,104	19		1.72	1.60
Prostatectomy	1,939	11	13.5	0.56	0.46
Operations other than simple cystostomy	922	5	2.3	0.54	0.54
Colon	2,389	20	9.0	0.83	0.48
Abdomen					
Exploration		8	3.7		
Paracentesis	321	1	0.5	0.30	0.30
Appendix	12,356	5	2.3	0.04	0.02
Kidneys	3,635	5	2.3	0.10	0.10
Rectum	1,952	5	2.3	0.25	0.25
Spleen	317	4	1.9	1.26	0.00
Subdiaphragmatic abscess	29	1	0.5	3.40	3.40
Omentum (tumor)	2	1	0.5	50.00	50.00
Small bowel	991	3	1.4	0.30	0.30
Ventral hernia	1,235	4	1.8	0.30	0.30

TABLE 2—*Cases of Fatal Embolism Resulting from Extra-Abdominal Operations*

Region of Operation	Cases
Hernia	14
Breast	8
Spinal cord	3
Long bones (reduction of fracture)	3
Long bones (open operation)	2
Chest (aspiration)	2
Minor gynecology	2
Trifacial nerve (avulsion for neuralgia)	1
Brain	1
Spine	1
Thyroid	1
Axillary glands	1
Face (plastic operation)	1
Rib (resection)	1
Arm (amputation)	1
Left hip (operation for tumor)	1

In the forty-three cases in which fatal embolism occurred following extra-abdominal operations, herniotomy was performed in fourteen, operation on the breast in eight, on the spinal cord in three, and on the long bones in two, aspiration of the chest in two and the reduction of fracture of long bones in three (table 2).

The deaths in the series of fatal cases of embolism represent 6 per cent of all deaths following operations during the last ten years. On the other hand, in a complete analysis of deaths resulting from opera-

tions during 1925, one period was found in which 2,606 consecutive operations were performed without a single proved case of pulmonary embolism. These operations did not include operations on the nose and throat, hemorrhoidectomy, aspiration, transfusion or similar surgical procedures.

Definite postoperative infections, such as infected wounds, pyelonephritis, miscellaneous abscesses, acute pericarditis or peritonitis had occurred in ninety-nine cases (44 per cent of the series). It should be remembered that these infectious conditions brought about the added complication of a more prolonged convalescence in bed for the patients. Twenty-nine of them had postoperative bronchitis and twenty-eight had postoperative phlebitis or symptoms suggestive of this condition. The average interval between the date of operation and the date of death was fourteen days. In sixty-nine cases, death was described as occurring suddenly, in thirty-four others it occurred within ten minutes of the first seizure, in twenty-two, within thirty minutes, in ten, within one hour, in fifteen, within twelve hours, in twenty-five, within twenty-four hours, in twenty-three, within seven days, and in six, within fourteen days, in nineteen, the time of seizure could not be established.

Obstruction of one of the large branches of the pulmonary artery is of course, a swift and hopeless tragedy for those patients in whom it is followed by death. Patients who are able to recover partially, however, from the shock caused by a large embolus, only to die from failure of circulation if left unaided, have a chance to be treated by supportive and sometimes effective therapeutic measures. The possibility of saving the patient's life by an emergency operation, that is, removal of the clot must be considered. This has been carried out successfully by Kirschner.¹ Two patients with unilateral pulmonary embolism have recently been treated successfully in the clinic by prompt administration of oxygen with the Barach-Roth tent. The subjective relief was almost immediate in both cases. Unfortunately, many patients who successfully withstand the first attack of embolism succumb to the second attack or to secondary pulmonary suppuration or pneumonia.

In fifty-six cases, forty-four surgical and twelve medical. In pulmonary embolism was found at necropsy, it was not regarded as the proximate cause of death. In most of these none of the usual clinical signs of embolism had manifested themselves and the condition was unsuspected. In most instances death was due to gradual extension of the embolus from myocardial degeneration, peritonitis, pneumonia or other causes. The emboli that were found were mostly small and appeared in the picture only as a terminal event.

¹ Kirschner, M. Ein durch die Treibhaken verursachter Embolus in der Arteria pulmonalis. *Arch. f. klin. u. exp. Med.* 135: 211, 1925.

In the nonsurgical group of forty-six cases (table 3), three patients with adenomatous goiter with hyperthyroidism and one with exophthalmic goiter, all of whom had myocardial degeneration, died from cardiac failure with decompensation. Nineteen other cases in this group were primarily cardiovascular, sixteen of them with marked decompensation. In half of the group of nonsurgical cases, therefore, death was accompanied by gradual cardiac failure. Although the emboli in many of these cases were small and relatively insignificant in their effects, their occurrence again emphasizes the importance of the condition of the circulatory system in bringing about thrombosis and embolism. It should be remembered that some of these apparent emboli may have been formed *in situ*.

TABLE 3—Deaths from Pulmonary Embolism in Nonsurgical Cases

Cause	Deaths
Hyperthyroidism with adenomatous goiter	3
Exophthalmic goiter	1
Cardiovascular disease	19
Carcinoma of stomach	3
Carcinoma of ovary	3
Carcinoma of prostate	1
Carcinoma of uterus	1
Carcinoma of rectum	1
Cyst adenoma of ovary	1
Fibromyoma of uterus	1
Retroperitoneal lymphosarcoma	1
Retroperitoneal tumor	1
Pyelonephrosis	2
Hypertrophy of prostate	1
Fractures, multiple	1
Gangrene of leg	1
Cellulitis of face	1
Peritonitis	1
Pemphigus	1
Acute yellow atrophy of liver	1
Sciatica	1

The factors, other than slowing of the circulation, that are commonly regarded as concerned in the production of thrombosis are changes in the composition of the blood and injury to the vessel wall. The former has been considered by Allen² and Snell³. Thrombosis within veins that have been cut is a normal occurrence and necessary to the completion of any surgical procedure. This should extend within the vessel to the point of entrance of the next tributary vein, when it extends beyond this point into the larger vessels, a pathologic condition of grave peril is created, as portions of the clot may become detached in the blood stream. It is interesting to note that the source of emboli is often some distance from the operative site.

2 Allen, E. V. Changes in the Blood Following Operation, *Arch Surg*, published in this issue.

3 Snell, A. M. The Relation of Obesity to Postoperative Pulmonary Embolism, *Arch Surg*, published in this issue.

Thrombosis, which may have served as the possible source of emboli, was found in 189 of the total series of 313 cases. In some instances two or even three of these sites of thrombosis were found in the same case. The four most common sources (table 4) were the iliac vein in sixty-four cases, the femoral vein in fifty-five, the pelvic veins in forty-three and the prostatic plexus in eighteen. Seventy-nine per cent of the sites of thrombosis were in these situations. The groups in which the probable source of emboli was in the iliac or femoral veins were studied further. In 14 per cent of these cases, operation had not been performed, in 15 per cent, the operation had been extra-abdominal, in 25 per cent it had been performed in the upper part of the abdomen, in 46 per cent, in the lower part of the abdomen. In only one case had operation been performed on the lower extremity—open operation for

TABLE 4—*Source of Emboli*

Source	Number
Iliac vein	64
Femoral vein	55
Pelvic veins	43
Prostatic plexus	18
Vena cava	15
Right auricle	10
Renal vein	7
Axillary vein	3
Right ventricle	3
Ovarian veins	3
Hemorrhoidal veins	1
Deep epigastric vein	1
Jugular vein	1
Vaginal plexus	1
Cervical plexus	1
Subclavian vein	1
Innominate vein	1
Azygos vein	1

fracture of the neck of the femur. Only two of the eighteen patients with thrombosis of the prostatic plexus had undergone prostatectomy. These statistics would indicate that the site of operation is not of paramount importance in determining the site of thrombosis and the source of emboli.

In only one case in the series was the probable source determined to be in the subclavian vein, and in three cases, in the axillary veins. Such factors as posture, stagnation of blood in dependent parts, decreased movement probably account for the more frequent occurrence of thrombosis in the veins of the pelvis and of the lower extremities than in the veins of the upper extremities. In order to counteract these factors, patients are encouraged to change their position frequently, passive and active movement of the extremities, and to breathe deeply since the principal force for the flow of blood through the large abdominal veins is the negative pressure created in the chest during inspiration. In order to counteract

and facilitate deep breathing, patients who on account of age or obesity are regarded as being more susceptible to embolism are supplied with elastic abdominal belts. The support supplied by these belts when the patient has to cough is also gratifying.

Some previous impressions regarding pulmonary embolism have been shown by this review to be without foundation. One such impression was that there was probably a seasonal variation in the incidence, in other words, that there were more cases in the spring and autumn months. In this review, however, it was found that although there was some monthly variation during a single year, there was but little change from month to month when the period of ten years was considered as a whole.

SUMMARY

The incidence of fatal pulmonary embolism among the surgical cases that came to necropsy at the clinic during the last ten years is 6 per cent. Patients at the clinic who die from pulmonary embolism are older than the average surgical patient, they are somewhat overweight, and, as a group, have a normal or somewhat subnormal blood pressure, a high percentage have postoperative infections.

While the importance of the operative procedure in determining the site of thrombus formation and the occurrence of pulmonary embolism cannot be overlooked, other factors, such as age, weight, general condition of the patient, efficiency of the circulation, bodily inactivity incident to almost any operative procedure and infection, should also be emphasized.

THE RELATION OF OBESITY TO FATAL POST-OPERATIVE PULMONARY EMBOLISM*

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The present study of the causes of postoperative death of obese patients was undertaken to determine, if possible, the cause of the increase in mortality in such patients and what measures might be taken to reduce it. This involved a comparison of the causes of death of obese patients with those of a control group. The latter was made up of all patients who died following operation during the same period, without regard to weight.

BASIS OF STUDY

The history of the patient in all cases of death after operation during a period of six years (from 1920 to 1925, inclusive) was studied. A total of 156 of these patients were definitely obese. In 145 cases of this group, necropsy was performed, in the remaining eleven, the clinical cause of death seemed sufficiently clear to permit their inclusion in the group.

The obesity in these 156 cases was graded from 1 to 4. 1 indicated slight obesity (from 20 to 35 pounds [9.0 to 15.9 Kg.] overweight), 2, moderate (from 35 to 60 pounds [15.9 to 27.2 Kg.] overweight), 3, marked (from 60 to 100 pounds [27.2 to 45.4 Kg.] overweight), and 4, extreme (more than 100 pounds [45.4 Kg.] overweight). The cases were divided into four groups according to this grading. Standard actuarial tables of weight were used as a basis for the classification. The percentage of incidence of peritonitis, pneumonia and other diseases in each group was compared with the percentages of each of these complications in the whole series of 1942 cases in which necropsy was performed.

As several possible causes may co-exist in the same case, the "principal cause of death" given on the death certificate was used as a basis for classification, consequently the figures concerning the incidence of peritonitis, pneumonia and other diseases shown in table 1, which gives the causes of postoperative death of obese patients, require an explanation. All cases of fatal pulmonary embolism, abdominal, cerebral, and peripheral vascular disease, and other causes are included under miscellaneous causes. These deaths form a distinct clinical group.

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Peritonitis, pneumonia and pulmonary embolism are the three major causes of postoperative death in the control group and in the group of obese patients. The experience of the Mayo Clinic, from 1920 to 1925, inclusive, was that these three causes accounted for 40 per cent of all postoperative deaths, pneumonia was the principal cause in 13.8 per cent, peritonitis, in 18.3 per cent and pulmonary embolism, in 7.9 per cent of all cases which came to necropsy. The figures for pneumonia and peritonitis are substantially the same in the group of obese patients as in the control group, pulmonary embolism, however, was about three times as frequent a cause of death in the former as in the latter. Embolism accounted for death in 20 per cent of the fatal cases in groups 1 and 2 (patients from 20 to 60 pounds overweight) and in

TABLE 1—*Causes of Postoperative Death in Obese Persons*

Group	Peritonitis			Pneumonia		Embolism		Thrombosis		Sepsis		Jaundice		Unexplained		Miscellaneous	
	Cases		Percentage	Cases		Cases		Cases		Cases		Cases		Cases		Cases	
	Oases	Oases		Percentage	Percentage	Percentage	Percentage	Percentage	Percentage	Percentage	Percentage	Percentage	Percentage	Percentage	Percentage	Percentage	Percentage
Group 1 slight obesity (from 20 to 35 pounds overweight)	40	7	17.5	4	10.0	10	25.0	1	2.5	4	10.0	3	7.5			11	27.5
Group 2 moderate obesity (from 35 to 60 pounds overweight)	62	13	21.0	10	16.2	12	19.3	5	8.1	7	11.3			1	1.6	14	22.6
Group 3 marked obesity (from 60 to 100 pounds overweight)	47	9	19.2	2	4.2	16	34.0	2	4.2	4	8.5	1	2.1	7	14.9	6	12.8
Group 4 extreme obesity (100 pounds or more overweight)	7	4	57.0			2	28.6									1	14.3
Total	156	33	21.2	16	10.3	40	25.6	8	5.1	15	9.6	4	2.6	8	5.1	32	20.6

about 30 per cent in groups 3 and 4 (patients more than 60 pounds overweight). Thrombosis of cerebral and abdominal vessels (a relatively infrequent cause of postoperative death) was found in 5 per cent of the obese patients. The percentage of incidence of the major causes of death in the group of obese patients is contrasted graphically in chart 1 with that in the control group.

The cases were analyzed in detail in order to determine any possible causes for this remarkably high incidence of fatal thrombosis and embolism in patients who were overweight. The significant observations on the forty obese patients who died from pulmonary embolism are summarized in table 2. The patients were divided into four groups similar to those in table 1. Twenty-two of the patients were women and eighteen were men, the average age of the former being 53 and of the latter, 56. In spite of the rather advanced age of the patients, clinical evidence of degenerative cardiac, vascular or renal changes was rather

infrequent. The blood pressure was usually within normal limits. In four cases the diastolic pressure was more than 100 mm., in seven the systolic pressure was more than 160 mm. In one case, cardiac enlargement was graded 2, in another there were significant electrocardiographic changes (T wave negativity in derivations I, II, and III). In both instances the blood pressure was normal. Definite evidence of renal insufficiency was not presented in any case. Phlebitis was noted as a postoperative complication in five cases. The weight had been reduced prior to operation in only two cases and in one of these 37 pounds (16.8 Kg.) had been lost by active reduction of weight in the hospital, in the other, 30 pounds (13.6 Kg.) had been lost in two years at home. About half of the cases of fatal pulmonary embolism in this

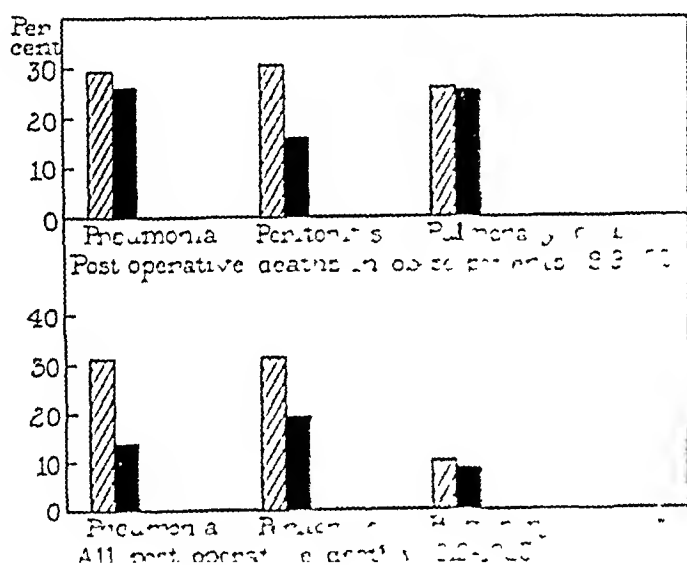


TABLE 2—Analysis of Cases of Fatal Pulmonary Embolism

Group 1—Patients from 20 to 35 Pounds Overweight											
Case	Sex	Age, Years	Weight Pounds	Blood Pressure		Operation	Anesthetic	Phlebitis	Days After Operation	Manner of Death	Reduction of Weight before Operation
				Sys	Diastolic						
1	♀	31	160	138	76	Removal of carcinoma of right breast	No record	None	22	Gradual, from repeated embolism	None
2	♀	60	167.5	110	80	Exploratory (inoperable ovarian tumor)	Procaine (local) nitrogen monoxid	None	3	Sudden	None
3	♀	33	153	108	74	Left nephrectomy	Ether	None	8	Sudden	None
4	♂	60	185	190	80	Suprapubic cystostomy	Ether	None	22	Gradual from multiple septic infarcts	None
5	♀	53	172	144	88	Suprapubic cystostomy for carcinoma of bladder	Ether	Present	28	Sudden	None
6	♂	53	187	128	80	Enterocenterostomy for carcinoma of bowel	Ether	None	9	Sudden	None
7	♂	70	198	105	66	Suprapubic cystostomy	Ether	None	5	Sudden	None
8	♀	40	158	170	110	Cholecystectomy and appendectomy	Ether	None	11	Sudden	None
9	♀	49	171	140	96	Laminectomy for tumor of the cord	Ether	None	3	Sudden	None
10	♂	71	198	136	89	Colostomy for carcinoma of rectum	Ether	None	21	Sudden	None
Group 2—Patients from 35 to 60 Pounds Overweight											
11	♀	67	170	146	74	Vaginal hysterectomy	No record	None	13	Gradual	None
12	♂	63	202	160	90	Suprapubic prostatectomy	Ether	None	18	Sudden	None
13	♂	55	220	140	90	Suprapubic prostatectomy	Procaine (spinal)	None	15	Sudden	None
14	♀	53	190	160	90	Repair of large umbilical hernia	Procaine	None	6	Sudden	None
15	♂	64	210	148	98	Suprapubic prostatectomy	Procaine	None	7	Sudden	None
16	♂	70	194	182	110	Suprapubic cystostomy	Procaine	None	11	Gradual, from repeated embolism	None

at the Mayo Clinic in this matter, failed to find any relation between the various types of anesthetic and the incidence of postoperative embolism. The present series is too small to permit of any conclusions in regard to seasonal incidence.

The duration of life after operation varied from three to fifty days, the average being about thirteen days. As might be expected, death was sudden in most cases (thirty), in five cases, gradual failure was noted, and in five, repeated pulmonary infarctions occurred. In the latter group the patients survived the operation from ten to twenty-two days, and died with clinical symptoms suggesting bronchopneumonia.

TABLE 3—*Analysis of Cases of Fatal Postoperative Thrombosis*

Case	Sex	Age, Years	Weight, Pounds	Obesity, Degree	Anesthetic	Operation	Site of Thrombosis	Days after Operation	Manner of Death
1	♂	33	175	1	Ether	Choledochostomy	Portal vein	12	Sudden collapse after stormy post-operative course
2	♀	42	180	2	Ether	Excision of cancer of right breast	Cerebral artery	8	Gradual
3	♂	76	200	2	Procaine, ether	Gastro-enterostomy for carcinoma of stomach	Coronary artery, pulmonary artery	9	Sudden
4	♀	40	205	2	Procaine, ethylene	Amputation of right arm for gangrene	Pulmonary, carotid and subclavian arteries	2	Gradual
5	♂	49	251	2	Ether	Right herniotomy	Mesenteric artery	3	Sudden
6	♀	42	218	3	Ether	Right temporal decompression for brain tumor	Superior longitudinal sinus	7	Sudden collapse after stormy course
7	♂	56	217	3	Ether	Splenectomy	Mesenteric vein	14	Gradual
8	♂	61	226	2	No record	Suprapubic prostatectomy	Inferior vena cava	120	Gradual

The relatively high frequency of fatal thrombosis is interesting although the factors that favor pulmonary embolism may not be operative in this group. Eight patients, approximately 5 per cent of the obese patients, died from this cause. The details of these cases are given in table 3. In one case, mesenteric thrombosis followed splenectomy, in another, thrombosis of the superior longitudinal sinus followed cranial decompression, in a third case, the presence of thrombosis of the subclavian artery had been determined before the arm was amputated. A fourth patient, aged 76, died from coronary thrombosis following operation. It is difficult to see how obesity could have had anything to do with the unfavorable outcome in these cases. The fact that in eight cases in the obesity group death was traced to thrombosis does not necessarily imply a relation between thrombosis and obesity.

CONCLUSIONS

The high incidence of pulmonary embolism as a cause of post-operative death in obese patients is of much interest. It suggests, but does not prove, that obesity, per se, increases the liability to this much feared complication. The average age in the group of 156 patients was 55, this emphasizes the relation between age and pulmonary embolism, previously noted by Lindsay² and Lister³. Difficulty of operation with unusual trauma may be a factor, mild circulatory failure with resultant venous stasis might conceivably be more common in obese persons. After operation on obese patients, there may be an increased liberation of thromboplastic lipid substances such as kephalin due to the extensive areas of fat invaded. True fat embolism, however, occurred in only two of the cases.

In interpreting the foregoing data one must bear in mind that there are no statistics available with regard to mortality and causes of death for particular operations according to age groups. These would serve as much more accurate controls than the whole groups of patients of all ages considered without respect to the type of operation. An analysis of the outcome of serious and extensive surgical procedures in older patients might well show a high incidence of fatal postoperative pulmonary embolism.

Observations on arterial and venous pressure and rate of circulation and studies of peripheral blood flow would probably shed much light on the subject of circulatory stasis, which is generally recognized as an important factor in the development of embolism. At the present time a definite regimen, designed to improve the general circulation and to combat venous stasis, is being tried at the Mayo Clinic under controlled conditions. Walters⁴ has been interested in the use of thyroid extract in this connection, and has recently reported favorably on its use.

SUMMARY

Pulmonary embolism following operation seems to be a more common cause of death of the obese patient than of the average patient. Whether this is due to the age of the patient, to the type of operation performed, to unknown factors related to the flow and coagulability of blood or to the obesity per se, cannot be definitely stated. From

2 Lindsay, E. C. The Prevention and Treatment of Pulmonary Embolism. *Lancet* 1: 527, 1925.

3 Lister, W. A. Causation of Pulmonary Embolism Following Operation. *Lancet* 1: 111, 1927.

4 Walters, Walman. The Suggested Use of Thyroid Extract in the Treatment of the Incidence of Postoperative Embolism. *Minnesota Med.* 10: 25, 1927.

consideration of my statistics and those presented by Henderson,⁵ it seems probable that there is a group of patients over 50 years of age, obese and with normal or subnormal blood pressure, who are particularly susceptible to pulmonary embolism as a postoperative complication

5 Henderson, E F Fatal Pulmonary Embolism A Statistical Review,
Arch Surg, published in this issue

POSTOPERATIVE PHLEBITIS

A CLINICAL STUDY^{*}

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This study is based on eighty-seven cases of postoperative phlebitis that I have observed. Information and exact data were sought to determine the following points: (1) the minimal signs and symptoms on which to make a diagnosis of phlebitis, (2) the degree of disability consequent to this complication, (3) the etiology, predisposing factors, such as intercurrent infection, and seasonal incidence, and (4) the relationship, if such exists, of phlebitis to fatal postoperative embolism.

For a period of two years, I examined, as a routine, patients with pain, soreness or swelling in the legs following operation. The criteria for establishing a diagnosis of postoperative phlebitis were ill defined, and in many cases phlebitis was erroneously diagnosed, with an unnecessary attendant increase in the postoperative convalescent period. Many patients complained of sensations in the legs and hips after operation, varying from fatigue and soreness to sharp twinges of pain. One group of patients complained of the symptoms that occurred on getting up from bed, usually from the seventh to the tenth day after operation. Other patients experienced soreness in the gluteal, calf or lumbar groups of muscles. Several complained of soreness in the feet from standing. In most instances, phlebitis was considered the trouble, and the patients returned to bed for an additional period of rest, with the leg elevated and heat applied. As some of these patients did not have phlebitis, it was obvious that minimal standards for the diagnosis were indicated. Two cases of septic thrombophlebitis were observed, but they are not included in this study.

MINIMAL DATA FOR THE DIAGNOSIS OF PHLEBITIS

The diagnosis of phlebitis in the legs was based on: (1) the location of pain or soreness, (2) the presence or absence of edema, (3) the constitutional reactions. Tenderness along the course of the vein is the most important single sign of phlebitis, and the diagnosis cannot be made unless this symptom was present. A diagnosis was not made when edema and fever were absent, when present the latter two important corroborative signs. The presence of pulmonary embolism is significant, and occasionally directs attention to the possibility of phlebitis in the veins of the leg.

^{*} From the Division of Medicine, Mayo Clinic, and The Mayo Foundation.

The situation of the soreness in phlebitis is necessarily along the course of the vein affected (fig 1) Three points or areas in the leg were examined for tenderness One or more of these areas were tender on palpation in the definite cases of phlebitis The middle of the calf, or the lower popliteal area, was tender on palpation in 64 per cent of the eighty-seven cases, in 9 per cent, the calf and lower and upper femoral areas were tender, and in 27 per cent, the upper and lower femoral areas The right leg was affected in 16 per cent, the left, in 64 per cent and both legs, in 20 per cent of the cases Tenderness or subjective soreness was confined closely to the vein in a longitudinal direction Frequently the vein could be felt as a tender, hard cord Often deep pressure

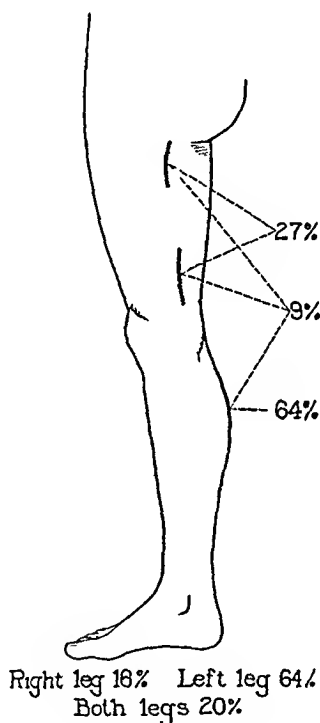


Fig 1—Points of tenderness in cases of postoperative phlebitis

was necessary to elicit pain, and often the patient could accurately trace the course of the vein by the subjective soreness Deep pelvic soreness was complained of in two cases, and was approximately localized to the vicinity of the iliac veins

Subjective Symptoms—The usual complaint was a localized, deep soreness, present during rest and often described as a deep, burning, dull ache, generally aggravated by moving the limb and by pressing on the tissues along the affected vessel

Edema—Demonstrable edema, graded 1 or 2, was present in 50 per cent of the cases A careful search was made for swelling over the malleolar and gluteal areas and the shin bone The absence of edema in half the cases would suggest that the thrombosis was limited to the more

superficial vessels, and to the short and long saphenous veins. The presence of adequate collateral venous circulation prevented fluid stasis. Seventeen per cent of the patients who had been afflicted with edema had a slight residual edema at the time of their dismissal. The massive brawny form of edema and phlegmasa alba dolens were not observed.

Systemic Reactions—Fever was present in some degree in 89 per cent of the cases. The mean temperature was 100 F (± 0.8); the highest was 104 F. In ten cases there was no fever. The average duration of fever was three and one-half days, ranging from one to ten days in the uncomplicated cases. The mean fever was determined in the cases of phlebitis without pulmonary infarction and in those with infarction; in the former group the mean maximal temperature was 100.5 F (± 1), in the latter, the mean temperature was 100.6 F (± 1.4). The probable error of these mean temperatures eliminated any difference between the fever in the two groups. In the group with pulmonary infarction, the range of duration was from one day to three weeks. The pulse rate was not greater than 100 in the majority of cases. The leukocyte response was slight, the count averaging 11,000 for the group, which is about the normal postoperative value. The highest count was 19,500 for each cubic millimeter. The average leukocyte count in the uncomplicated cases of phlebitis was 9,000 for each cubic millimeter; that in cases with pulmonary infarction was 13,500 for each cubic millimeter.

Pulmonary Complication—Pulmonary infarction was recognized clinically in twenty-nine cases (33 per cent). The signs and symptoms of the condition were usually typical, consisting of pleuritic pain, slight hemoptysis with a demonstrable area of impaired resonance and friction rub. The signs and symptoms of infarction appeared on an average of four days after the onset of phlebitis, but in three cases they preceded the signs of phlebitis. The mean maximal rise in temperature in this group was 100.6 F (± 1.4), and the average duration of fever was five days, ranging from one to twenty-one days. In no instance was there sufficient pleurisy with effusion to require paracentesis. The results of roentgenologic examination were frequently negative or "evidence of congestion or bronchopneumonia" was reported. Pulmonary infarction was not a complication, nor was serious disability noted as a result of the pulmonary infarction. The usual clinical diagnosis was bronchopneumonia from pulmonary infarction.

DEGREE OF DISABILITY

The degree of disability as a result of phlebitis was slight in all of the eighty-seven cases. In only two cases was serious disability noted in the months

ETIOLOGY

Evidence pointing to the direct cause of the phlebitis was not obtained. The signs and symptoms indicated an infectious lesion of the wall of the vein and secondary thrombosis. A study of resected segments of veins in superficial types of phlebitis revealed marked inflammatory

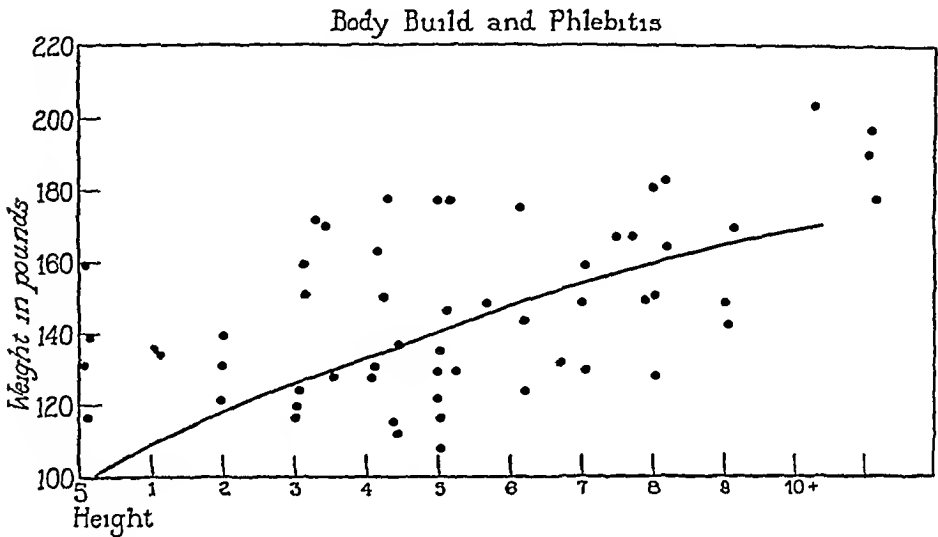


Fig 2—Cases of phlebitis charted according to weight and height, distribution rather even for all builds

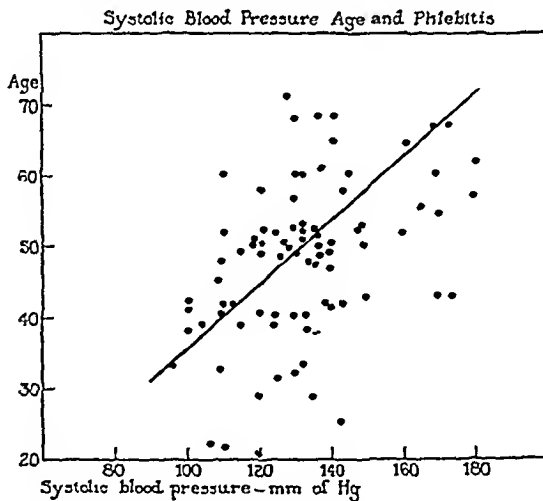


Fig 3—Incidence of phlebitis with regard to the systolic blood pressure at various ages. The majority of cases are within the normal range of pressure for the age.

reaction in all coats of the vein and the contiguous tissue. The vessel was markedly infiltrated with polymorphonuclear leukocytes. The obturating thrombus was composed of erythrocytes, leukocytes and fibrin. The reaction was intense and suggested an inflammatory process on an infectious basis.

Possible Predisposing Factors—Sixty-six per cent of the patients in the series were women and 34 per cent were men. The ages varied from 18 to 72 years. The mean age for the group was 47.1 (± 0.8) years. The mean weight was 151.6 (± 1.7) pounds, and 15 per cent of the patients were definitely obese. There was no demonstrable correlation between phlebitis and body build in the curves on weight and height (fig. 2). The factors of age and systolic blood pressure were considered in relation to phlebitis (fig. 3). The mean systolic pressure was 131.5 (± 1.3). Correction was not made in the systolic blood pressure for age, weight and sex. It will be seen that while the greatest incidence was between the fifth and sixth decades, the majority of cases fall within the range of blood pressure that was normal for the age.

Types of Preceding Operation—Phlebitis followed operations of the intra-abdominal type in 84.5 per cent of the cases, fifteen and one-half

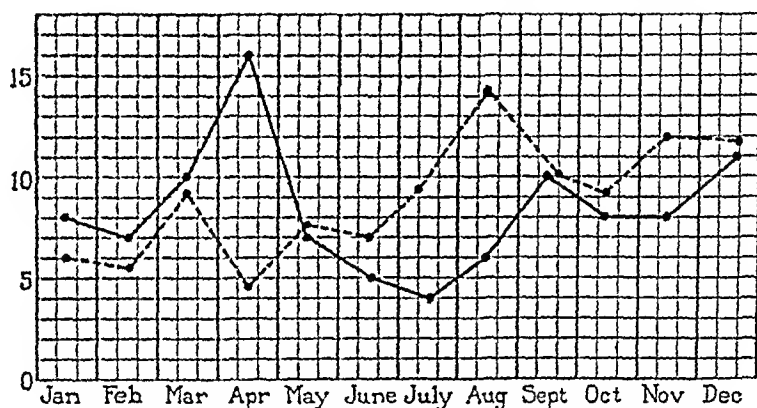


Fig. 4—Monthly percentage incidence of cases of phlebitis, from 1923 to 1925, inclusive, contrasted with monthly incidence of fatal cases of pulmonary embolism. The solid line indicates cases of phlebitis, the broken line, cases of embolism.

per cent were extraperitoneal, 40 per cent of the abdominal operations were performed on the pelvis and 60 per cent on the stomach, gall-bladder and appendix. There was one instance of phlebitis following removal of the breast.

SEASONAL INCIDENCE

There has been a clinical impression that phlebitis has a seasonal incidence. Figure 4 shows the monthly incidence of the cases from 1923 to 1925 inclusive, with the monthly incidence of fatal cases of pulmonary embolism for the same years. The incidence curves are not comparable. Figure 5 gives a more detailed graphic analysis. The number of surgical entrants to St. Mary's Hospital is shown for each month from 1923 to 1925. The number of cases of fatal postoperative

embolism and postoperative phlebitis are shown for the same periods. It will be observed that in about half the months there is a rough correlation between the greatest number of surgical entrants and the highest incidence of pulmonary embolism. Such a correlation apparently does not exist between the surgical entrants and the cases of phlebitis. Figure 6 shows curves for the total number of cases of embolism and phlebitis and surgical entrants for the three year period. The curves for the cases of embolism and surgical entrants show some relationship,

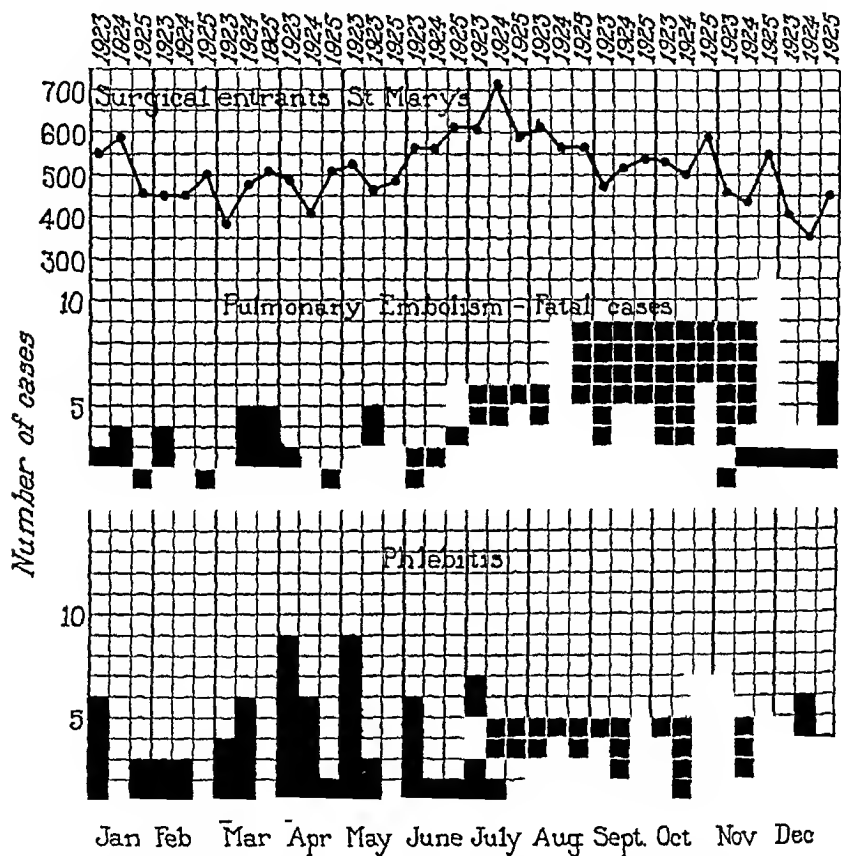


Fig 5—Comparison of surgical entrants with incidence of pulmonary embolism and of phlebitis by monthly periods for three years

while the curve for the cases of phlebitis seems to be independent of the curve of the surgical entrants. There is a spring and fall incidence producing two peaks in the curve for phlebitis which is different from the curve for postoperative embolism.

RELATIONSHIP OF POSTOPERATIVE PHLEBITIS TO EMBOLISM

Henderson showed in his study on postoperative fatal pulmonary embolism that probable phlebitis was present in twenty-nine cases (11 per cent). This incidence of phlebitis is probably higher than the actual

incidence as the minimal standards for its diagnosis was not carried out in many of his cases. In my series of eighty-seven cases of phlebitis, fatal pulmonary embolism did not occur once, while pulmonary infarction was recognized in 33 per cent. It is probable that if the chest were carefully examined in every case of phlebitis, regardless of whether the chest produced symptoms, the incidence of pulmonary infarction would be higher.

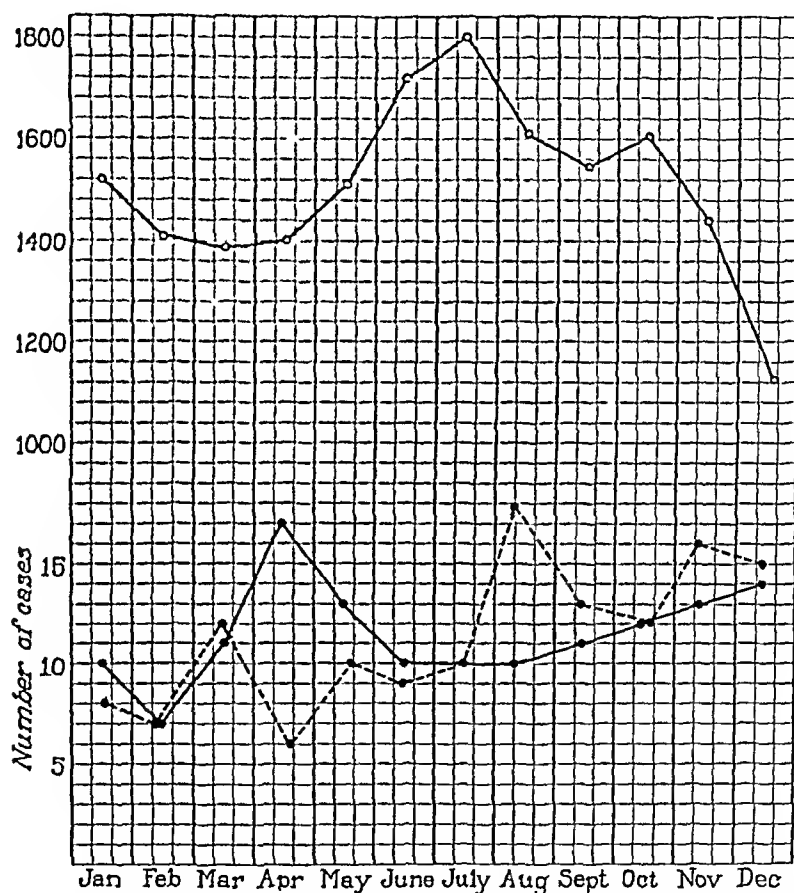


Fig 6—Comparison of surgical entrants with incidence of postoperative phlebitis and of postoperative embolism during the years 1923, 1924 and 1925, monthly average for three years. The solid line indicates cases of phlebitis, the broken line, cases of embolism.

TREATMENT AND PROGNOSIS

The treatment of phlebitis has consisted of elevation of the involved limb, heat applied locally and enforced rest. The average length of time for treatment was fourteen days. In 17 per cent of the cases there was some residual edema at the time of the patient's dismissal. These patients were advised to carry out postural exercises, as for obliterative arterial disease. They consist in elevation of the leg to 180 degrees for one minute, lowering it for one minute, then letting it rest in a horizontal

position for two minutes. These exercises are repeated ten times, and the series is repeated two or three times daily until the postural edema has disappeared. If these measures do not suffice, bandaging is advised. The cloth elastic bandages are applied from the foot to the middle of the thigh in the morning before the patient arises, and they are changed at least three times daily. In only two cases did signs of edema persist longer than six months.

The treatment of pulmonary infarction consists in strapping the chest for the pleuritic pain, administering opiates and prescribing an additional period of rest. Serious sequelae from the pulmonary complication were not noted in the cases in this series.

COMMENT

The diagnosis of postoperative phlebitis is too frequently made on insufficient signs and symptoms. The existence of pain or soreness in the leg is the usual basis for diagnosis. Exact localization of the tender or painful area will usually indicate whether the vein is the seat of the trouble. Tender palpable areas were noted in a series of eighty-seven cases, and these were fairly well limited in three. Frequently the vein was palpated as a firm, tender cord. The diagnosis of phlebitis has more than an academic interest, as many days of additional time in bed may be prevented or more rigid treatment instituted if the diagnosis is certain. Pulmonary infarction is a common complication, while fatal pulmonary embolism is apparently rare. This verifies a surgical impression of the relative safety of phlebitis. The explanation for this must rest on the fact that phlebitis is an inflammatory lesion. The clot is firmly attached to the wall of the vein, and large fragments are not easily dislodged. Small fragments are thrown off and become lodged in the periphery of the lung, producing a sharp reaction in the parenchyma of the lung with resulting pleuritis and signs and symptoms of a localized bronchopneumonia. The dislodged thrombi in the cases of fatal embolism are larger, and frequently long segments are dislodged and carried to the lung. Their attachment to the wall of the vein is insecure, and dislodgment is easy. Further evidence on the probable essential difference in the nature and behavior of the cases of phlebitis and fatal embolism is shown by the seasonal incidence. The incidence curve of fatal pulmonary embolism seems to follow roughly the curve of the surgical entrants. Phlebitis suggests a seasonal incidence similar to that observed in duodenal ulcer. The spring and fall colds and infections of the upper respiratory tracts may be factors. While the pathologic appearance and the clinical course of phlebitis suggest an infectious origin, the bacteriologic agent is not proved. In a series of cases of idiopathic superficial phlebitis, culture of a portion of the inflamed vessel and contained clot have resulted negatively. No correlation has been determined to

exist between phlebitis and the factors of age, weight and systolic blood pressure, factors which seem to play a contributory rôle in cases of embolism as shown by Henderson and Snell

SUMMARY

In a series of eighty-seven carefully studied cases of postoperative phlebitis, the most characteristic diagnostic sign was a localized tenderness of the affected vein. The presence of edema is equivocal. Pulmonary infarction was a frequent complication, but no instance of fatal pulmonary embolism was encountered. Comparison of the seasonal incidence and predisposing factors in phlebitis and pulmonary embolism shows certain clear-cut differences. The degree of disability due to postoperative phlebitis was notably slight in this series of cases.

CHANGES IN THE BLOOD FOLLOWING OPERATION

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The relatively high incidence of vascular thrombosis leading to pulmonary embolism in surgical patients as compared with medical patients is well known, but the cause is still obscure. The implication is that the surgical procedures, per se, or their sequelae, are responsible for the occurrence of pulmonary embolism. Since primarily the embolus is a clot dislodged from some distant locus, attention is directed toward the mechanism of blood clotting and the factors that might

Cases Studied for Changes in the Blood Following Operation

Case	Age, Sex*	Height, Inches	Weight, Pounds	Operation	Post-operative Complications	Length of Operation, Minutes	Anesthetic
1	65, ♂	71	165	Andrews Bassini herniotomy	None	28	Regional
2	59, ♂	70	136	Posterior gastro enterostomy	None	45	Ethylene, oxygen and ether
3	47, ♂	72	188	Posterior gastro enterostomy	None	50	Ethylene, oxygen and ether
4	46, ♀	65	158	Cholecystectomy	None	50	Ethylene, oxygen and ether
5	43, ♀	—	195	Total abdominal hysterectomy	None	47	Ethylene, oxygen and ether
6	48, ♀	65	169	Cholecystectomy	Phlebitis	50	Ether
7	45, ♂	70	175	Andrews Bassini herniotomy	None	60	Ether
8	48, ♂	67	178	Bilateral Andrews Bassini herniotomy	None	45	Ether
9	31, ♀	62	168	Posterior gastro enterostomy	None	55	Ether
10	62, ♂	60	160	Cholecystectomy, posterior gastro-enterostomy	None	81	Ether
11	55, ♀	60	118	Cholecystectomy, appendectomy	None	40	Ether
12	44, ♀	66	160	Radical amputation of the breast	None	55	Ether

* In this table, ♂ indicates male, ♀, female

participate in the formation of a clot within a vein following operation. In order to determine what effect, if any, a major operation might have on the condition of the blood, twelve patients were observed for changes in the blood following operation at the Mayo Clinic (table 1). Five determinations were made of each factor studied. The first determination was made within two hours before operation, the second within four hours after operation, the third on the third day following operation, the fourth on the sixth day following operation and the fifth on the tenth day following operation.

OBSERVATIONS ON PATIENTS AFTER EXAMINATION

Erythrocytes—Erythrocytes were counted from capillary blood. With two exceptions, the decrease in erythrocytes occurred immediately after operation. In cases 3 and 7 the decrease occurred between the second and third readings. The decrease in the number varied between

200,000 in case 7 and 1,000,000 in case 2. The approximate average decrease for the entire group was 600,000 (12.5 per cent). The average weight of these patients was 75 Kg. The average volume of whole blood was 6,750 cc (90 cc for each kilogram of body weight). The amount of blood lost at operation which would cause a diminution of 600,000 erythrocytes then could be calculated as 843 cc (12.5 per cent of 6,750 cc). Obviously this loss does not occur in such simple operations as unilateral herniotomy. The observations on an additional group of fourteen patients show that the decrease in the number of erythrocytes immediately after operation is not as constant as is indi-

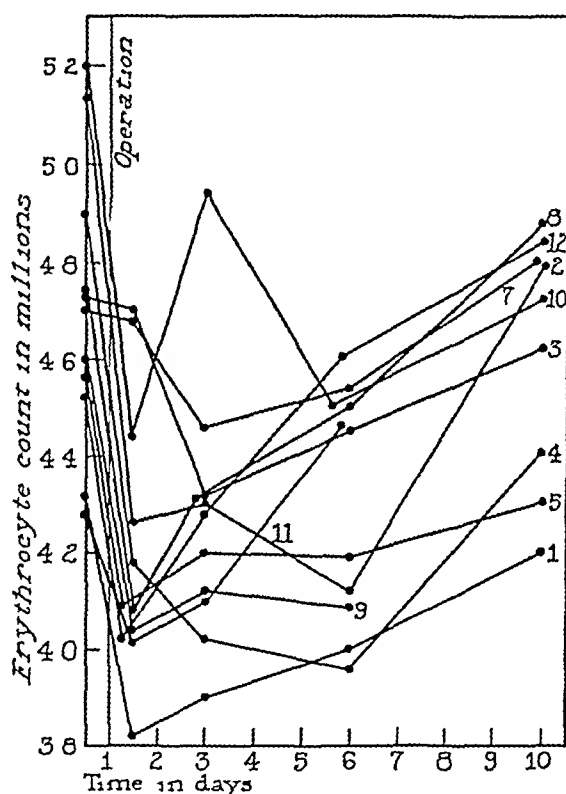


Chart 1—Change in the number of erythrocytes following operation

cated in chart 1. In some instances there was an immediate post-operative increase of 1,000,000 cells. The number of erythrocytes in oxalated blood drawn from the median basilic vein and from the capillary blood were practically identical. The increase in the erythrocytes was gradual, usually beginning at the second reading and being complete at the fifth. Many factors influence the number of erythrocytes, as has been shown by Bostrom,¹ Boycott and Jones,² Schneider

1 Bostrom, E. F. Conditions Causing an Unequal Distribution of Erythrocytes in the Blood-Stream, *Am J Physiol* **58** 195, 1921

2 Boycott, A. E., and Jones, C. P. The Influence of Anesthesia on the Restoration of the Volume of the Blood After Haemorrhage and After Transfusion, *Jour Path & Bact* **25** 335, 1922

and Havens,³ Scott and his co-workers,⁴ and von Lesser⁵ These investigators noted that the number of the erythrocytes was influenced by vasoconstriction, exercise, abdominal massage, abdominal pressure, changes in blood pressure, the anesthetic and the amount of blood lost at operation Their observations and this study indicate that many factors influence the number of erythrocytes following operation, among which peripheral vasomotor changes, changes in the blood pressure, rest in bed, trauma within the abdomen and abdominal bandaging are the most important

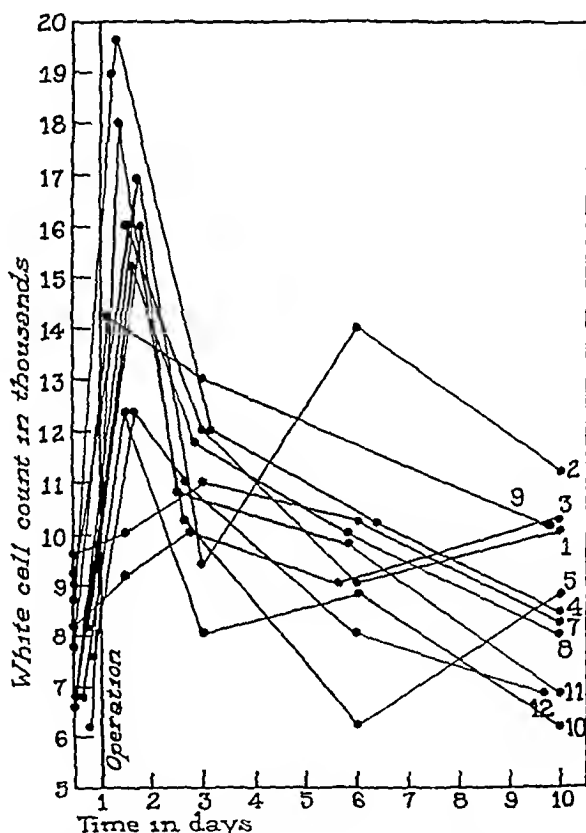


Chart 2—Change in the number of leukocytes following operation

Leukocytes—Leukocytes were counted in the capillary blood A marked increase was noted in the number of leukocytes for each cubic millimeter of blood at the second reading, except in cases 3 and 7 (chart 2) This increase varied from 11,500 cells in case 4 to less than

3 Schneider and Havens, quoted by Bostrom (footnote 1)

4 Scott, F H Factors Influencing the Interchange of Fluid Between Blood and Tissue Spaces I Blood Pressure, *Am J Physiol* 44 298, 1917
 Scott, F H, Herrmann, E T, and Snell, A M Factors Influencing the Interchange of Fluid Between Blood and Tissue Spaces II Muscular Activity, *Am J Physiol* 44 313, 1917

5 Von Lesser, quoted by Scott (footnote 4)

5,000 in case 12 the average increase was approximately 8,000 cells. The decline in the number of leukocytes was almost as abrupt as the increase, being marked between the second and third readings and more gradual between the third and fifth. An unexplained increase in the number of leukocytes occurred between the third and fourth readings in case 2. In most cases, return to the preoperative level was not complete until the fifth reading. That the leukocytes do not increase in the capillary blood alone is shown by data from fifteen additional patients from whom the blood was removed simultaneously from the ear and from the median basilic vein. The average postoperative increase of leukocytes in the venous blood was 12,500 and in the capillary blood 13,900. The number of leukocytes in the blood from the ear average 2,500 cells higher than in the venous blood. Discrepancies in the number of leukocytes in the capillary and venous blood have been studied by Yarbrough⁶ and Foord⁷. The factors that influence the number of leukocytes have been studied by Shaw,⁸ Mora, Amtman and Hoffman,⁹ Isaacs and Gordon,¹⁰ and Dawson.¹¹ From their observations and from the evidence derived from the study of this series of cases, it is probable that the consistent increase in the number of leukocytes following operation is due to many factors, the more important of which are the release of leukocytes from temporary "storage areas," peripheral vasoconstriction, the mental status of the patient and trauma to tissues.

Fibrin—Estimations of fibrin were made by the method of Foster and Whipple¹². There was a definite increase in two cases and a decrease in one case at the second reading. In all cases there was a

6 Yarbrough, Nancy. Blood Counts with Oxalated Blood, *J Lab & Clin Med* **7** 172, 1921.

7 Foord, A. G. Blood Counts With Oxalated Blood Compared With Ordinary Counts, *J Lab & Clin Med* **8** 343, 1922.

8 Shaw, A. F. B. Influence of Vasomotor State of Peripheral Blood-Vessels on Leukocytic Content of Blood, *J Path & Bact* **29** 389, 1926.

9 Mora, J. M., Amtman, L. E., and Hoffman, S. J. Effect of Mental and Emotional States on the Leukocyte Count, *J A M A* **86** 945 (March 27) 1926.

10 Isaacs, Raphael, and Gordon, Burgess. The Effect of Exercise on the Distribution of Corpuscles in the Blood Stream, *Am J Physiol* **71** 106, 1924.

11 Dawson, F. I. The Condition of the Blood After Operation and Fracture, *Edinburgh M J* **18** 426, 1905.

12 Foster, D. P., and Whipple, G. H. Blood Fibrin Studies. I. An Accurate Method for the Quantitative Analysis of Blood Fibrin in Small Amounts of Blood, *Am J Physiol* **58** 365, 1922, II. Normal Fibrin Values and the Influence of Diet, *ibid*, p. 379, III. Fibrin Values Influenced by Transfusion, Hemorrhage, Plasma Depletion and Blood Pressure Changes, *ibid*, p. 393, IV. Fibrin Values Influenced by Cell Injury, Inflammation, Intoxication, Liver Injury and the Eck Fistula, *ibid*, p. 407.

marked increase at the third reading (chart 3), this averaged approximately 175 mg for each hundred cubic centimeters of blood (41 per cent increase over the original average reading) The variation is more marked than that which occurs normally¹² The fibrin content between the third and fifth readings varied, increasing or decreasing slightly A marked increase was noted between the fourth and fifth readings in two cases The values were uniformly high on the tenth day, and there was no indication of a return to the preoperative level

After an intensive study of the effect of many factors, Foster and Whipple concluded that trauma to the tissues is the most powerful single stimulus to the overproduction of fibrin in the blood Schultz, Nicholes and Schaefer¹³ and Smotrov¹⁴ studied the influence of additional factors on the amount of fibrin Smotrov found high values in patients with syphilis, cancer and other conditions, and was convinced that the

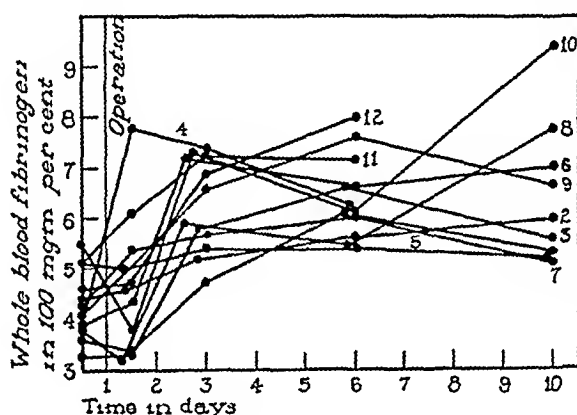


Chart 3—Changes in the amount of fibrin in the blood following operation

increase in fibrin is not due to the withdrawal from the liver but to a decomposition of albumin in many tissues This has not been the opinion of Foster and Whipple Smotrov could not demonstrate any relationship between the amount of fibrinogen and the time of coagulation of the blood, although the size and resistance of the clot seemed to parallel the amount of fibrin in the blood In view of the foregoing and the absence of wound infections, it would appear that the almost doubled amount of fibrin in the cases of this series was probably due to trauma, which may have produced a demand for an increase in fibrin at the site of the wound

Bleeding Time—There were no uniform variations in the bleeding time The divergent results probably indicate errors in calculation

13 Schultz, E W, Nicholes, J K, and Schaefer, J H Studies on Blood Fibrin Its Quantitative Determination, Normal Fibrin Values, and Factors Which Influence the Quantity of Blood Fibrin, *Am J Path* 1 101, 1925

14 Smotrov, V N *Russk khn Mosk* 3 843, 1925

Platelets—There were no uniform variations in the number of platelets. With the exception of case 6, in which the count was low at all readings, and that of case 7, in which it was uniformly high, the number of platelets was approximately normal, varying from 200,000 to 260,000.

Coagulation Time—Two methods for the study of the coagulation time were used, the older method of Lee and the more recent capillary-tube method of Petersen and Mills¹⁵. The results with the Lee method were variable and seemed of little significance. With the Mills method, there was an increase in coagulation time between the first and second readings in five cases and a decrease in three cases, there was a decrease between the third and fourth readings in all cases, except in cases 5 and 12. The results were widely divergent between the fourth and fifth readings (chart 4). Smotrov¹¹ and Nizner¹⁶ did not find any consistent

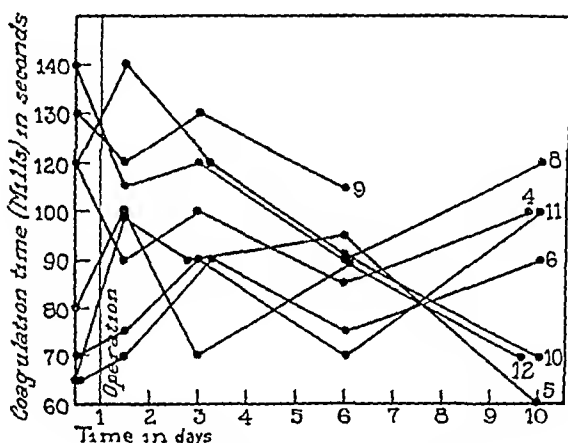


Chart 4—Change in coagulation time following operation

changes in the coagulability of the blood following operation. Nizner believed that the time of coagulation of the blood is variable, depending on such factors as hunger, catharsis, enemas and the patient's mental and physical state. He concluded that patients in whom the coagulation time of the blood is increased following operation are more liable to postoperative complications. This observation could not be confirmed in the small group of cases presented here. Straus and Rubin¹⁷ found a transitory but definite increase in bleeding and coagulation time following ethylene anesthesia. The changes in the coagulation time in this series of cases were slight and inconstant.

¹⁵ Petersen, M. F., and Mills, C. A. A New Method for Accurately Determining the Clotting Time of the Blood, *Arch Int Med* **32** 188 (Aug.) 1923.

¹⁶ Nizner, E. *Russk Klin Mosk* **1** 522, 1924.

¹⁷ Straus, D. C., and Rubin, H. H. The Coagulation Time in Ethylene Anesthesia, *J A M A* **88** 310 (Jan 29) 1927.

Blood Calcium—With the exception of cases 7, 8 and 9, there was a decrease in the amount of calcium in the blood at the second reading, varying from 0.4 to 1.0 mg for each hundred cubic centimeters (chart 5). A further decrease was noted in several cases at the third reading. In the remaining cases there was approximately the same amount of calcium at the third reading as at the second, except in cases 11 and 12, which showed increased amounts. There were no constant variations in the amount of calcium in the blood following the third reading. Sakaian found that narcosis alone did not produce any change in the calcium content of the blood. He also showed that great losses of blood during operation in some cases produced an increase in the amount of calcium and in others a decrease, associated with an increase or decrease in the coagulability of the blood. This relationship could

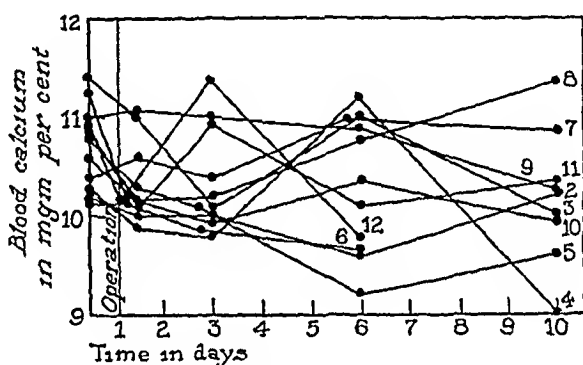


Chart 5—Change in the amount of calcium in the blood stream following operation

not be demonstrated in the cases of this series, and the changes in the amount of calcium in the blood did not seem great or constant enough to be of significance.

Prothrombin Time—The prothrombin time was calculated by the method of Howell¹⁸. The results in one case are shown in chart 6. The numbers on the curves indicate the tube number in the series. Each curve (for example, the first curve in chart 4) represents the variation in the prothrombin time on several days in a tube containing constant ingredients, the only known possible variation being in the quality (not quantity) of the blood introduced at successive tests. The results in the other nine cases are similar to those shown in chart 4, there was a sharp increase in the prothrombin time at some time following operation. In all cases the sharp increase was followed by an equally sharp decrease. If an increase in the prothrombin time indicates a decrease in the amount

¹⁸ Howell, W. H. The Condition of the Blood in Hemophilia, Thrombosis and Purpura. *Arch. Int. Med.* **13**: 76 (Jan.) 1914.

of prothrombin in the blood following operation, it might be explained on the basis of the utilization of prothrombin in the transformation of fibrinogen into fibrin

Lipoids and Cholesterol—Fatty acids were calculated by the method of Bloor, Pelkan and Allen¹⁹ In cases 1, 2, 3 and 7 no significant changes were observed In cases 5, 6 and 13 the readings were originally high but dropped rapidly between the first and fourth readings, and none reached the preoperative level by the tenth day (chart 7) The results in these three cases are of interest largely because all the patients were obese

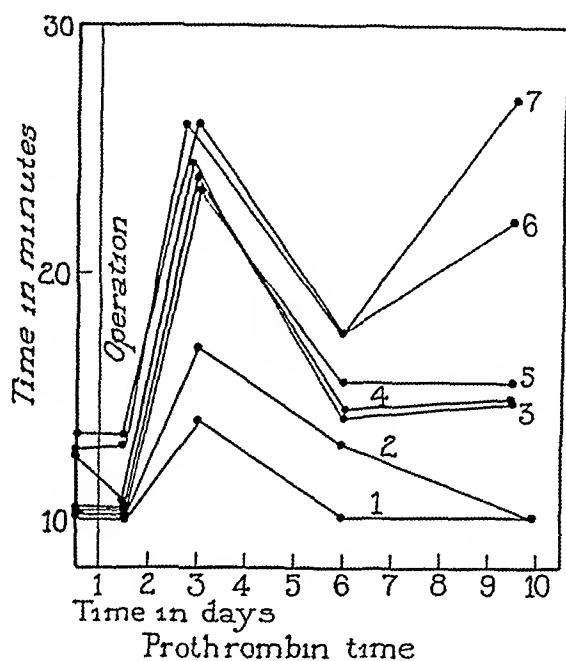


Chart 6—Change in prothrombin time in one patient following operation

Lecithin was determined by the method of Whitehorn²⁰ A sharp diminution in the amount of lecithin occurred in all cases (chart 8), in some cases between the second and third readings but more constantly between the third and fourth readings Results between the fourth and fifth readings were variable

The total fats were calculated by the addition of the values for the fatty acids and the lecithin There was a uniform decrease in the amount between the first and fourth readings (chart 9), it remained unchanged or increased slightly following the fourth reading, except in case 3

19 Bloor, W R, Pelkan, K F, and Allen, D M Determination of Fatty Acids (and Cholesterol) in Small Amounts of Blood Plasma, *J Biol Chem* 52 191, 1922

20 Whitehorn, J C A Method for the Determination of Lipoid Phosphorus in Blood and Plasma, *J Biol Chem* 62 133, 1924

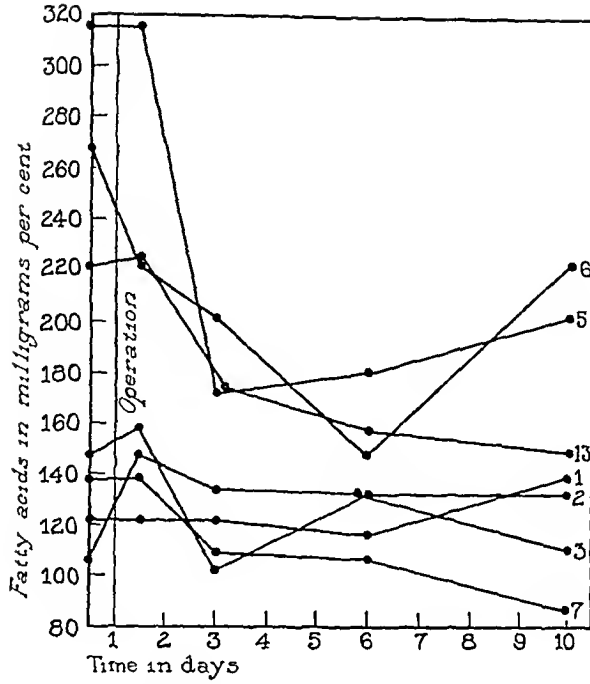


Chart 7—Change in the amount of total fats in the blood following operation

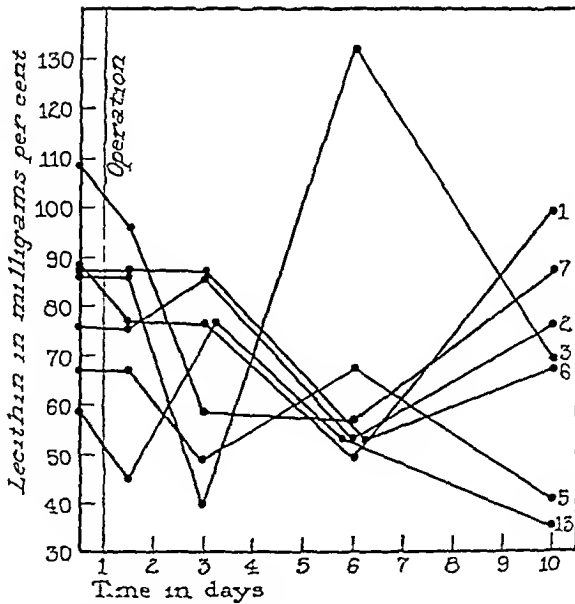


Chart 8—Change in the amount of lecithin following operation

The cholesterol content of the blood was studied by the Bloor²¹ method. There were no constant variations which could be considered significant.

Atkinson and Ets²² found that 1 gram (0.06 Gm.) of morphine sulphate given to dogs caused a decrease of 13 per cent of cholesterol and 9 per cent of lecithin, but increased the total fat 10 per cent. Bloor²³ could show no effect of morphine on the amount of total fat. In this series of cases, high fatty acid values in obese patients were sharply diminished following operation, the amounts of lecithin and total fats were definitely diminished and the cholesterol values were unchanged. Morphine narcosis alone probably could not account for these changes.

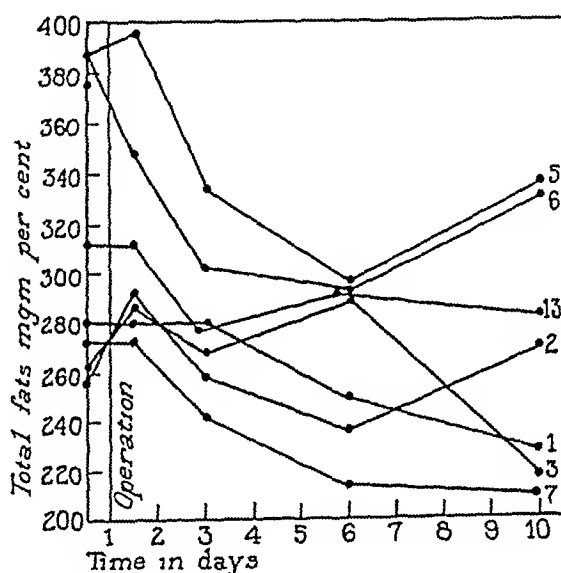


Chart 9—Changes in the amounts of total fats in the blood following operation

COMMENT

The number of platelets, the cholesterol, the bleeding time and the coagulation time (Lee) do not show definite change and do not require comment. The coagulation time (Mills) and the blood calcium show slight variations but not consistently enough to be considered of significance. The number of erythrocytes and leukocytes, the prothrombin time, the fibrinogen and the lipoids show definite and constant changes.

21 Bloor, W. R., and Knudson, Arthur. The Separate Determination of Cholesterol and Cholesterol Esters in Small Amounts of Blood, *J. Biol. Chem.* **27** 107, 1916. Bloor, W. R. Studies on Blood Fat. II. Fat Absorption and the Blood Lipoids, *J. Biol. Chem.* **23** 317, 1915.

22 Atkinson, H. V., and Ets, H. N. Chemical Changes of the Blood Under the Influence of Drugs. II. Morphine, *J. Lab. & Clin. Med.* **8** 170, 1922.

23 Bloor, W. R. Studies on Blood Fat. I. Variations in the Fat Content of the Blood Under Approximately Normal Conditions, *J. Biol. Chem.* **19** 1, 1914.

which are in sharp contrast to the other factors studied. Walters and Hendricks²⁴ have demonstrated similar variations in the fibrin, calcium, leukocytes and coagulation time. The fibrinogen is probably the most important of these changes. Essential as it is in the process of blood coagulation, the sharp constant increase following operation is doubtless significant in intravascular coagulation. The action of the fibrinogen may be manifested by the increased size and strength of the clot (Smotrov), although there is no apparent parallel change in the coagulation time. The postoperative increase in the number of leukocytes is significant because leukocytes are known to furnish thromboplastic substances that play an important part in the coagulation of the blood. The sharp prolongation of the prothrombin time is important, although the interpretation is obscure. The change in the number of erythrocytes may indicate widespread vasomotor disturbances which definitely influence intravascular clotting. The consistent decrease in the amount of the phospholipoid, lecithin and the total fats and the diminution of the fatty acids in obese patients are of interest, although their importance is not clear. The other papers in this series show the influence of many other factors on the occurrence of fatal pulmonary embolism. Studies by Johnson²⁵ and Brown²⁶ have shown that anesthesia and inflammatory postoperative phlebitis have little or no demonstrable influence on the occurrence of pulmonary embolism. Although this study is based on a small number of clinical and surgical types, it is apparent that changes in the blood were consistent in response to operation. It is probable that with the possible exception of the lipoids in the blood, there is a non-specific physiologic response to operation which occurs independently of the clinical or surgical status of the patient. This nonspecific physiologic change produces definite changes in the blood which may partially explain the relatively high incidence of pulmonary embolism occurring in surgical patients as compared with nonsurgical patients. There is probably in every surgical patient a definitely increased potentiality for intravascular coagulation by virtue of these changes, but this in all probability plays a minor part in comparison with other factors in the actual deposition of the clot and the subsequent pulmonary embolism.

24 Walters, Waltman, and Hendricks, W. A. Unpublished data.

25 Johnson, A. C. Unpublished data.

26 Brown, G. E. Postoperative Phlebitis, A Clinical Study, *Arch. Surg.* published in this issue.

PLASMA PROTEINS IN CUTANEOUS BURNS *

EDWARD C DAVIDSON, M D

AND

C W MATTHEW

DETROIT

Attention has frequently been called to the analogy between traumatic toxemia and the toxemia following extensive burns. Certain alterations in the plasma proteins have been observed which are of fundamental importance in explaining the syndrome in shock. It, therefore, seemed desirable to study the plasma proteins of a group of cases of burns to determine whether further light might be thrown on the toxemia which is seen after recovery from the initial collapse in such cases.

Starling¹ demonstrated that the walls of the blood vessels are normally impermeable to colloids. It is also known² that the composition of the plasma of a given person is relatively constant. Dale and Laidlaw³ have shown, however, that the concentration of blood in histamine shock is not accompanied by an increase of the plasma proteins. They concluded that histamine acted directly on the capillary endothelium, rendering it more permeable, and that whole plasma rather than simply water escaped into the tissues. Bodansky⁴ subsequently studied the plasma proteins in experimental anhydremia produced by histamine and reached the same conclusion. Gasser, Erlanger and Meek⁵ likewise observed filtration of whole plasma into the tissues in experimental traumatic shock.

Bayliss⁶ states that, since it is the osmotic pressure of the proteins that prevents the rapid filtering away of the liquid portion of the blood into the tissue spaces and causes reabsorption of fluid from them, it can be effective only as long as the concentration of the proteins is unequal on the two sides of the membrane. It is clear that if the proteins are

* From the Surgical Service of the Henry Ford Hospital.

1 Starling, E. H. On the Absorption of Fluids from the Connective Tissue Spaces, *J. Physiol.* **19** 312, 1895-1896.

2 Howe, P. E. The Function of the Plasma Proteins, *Physiol. Rev.* **5** 439, 1925.

3 Dale, H. H., and Laidlaw, P. P. Histamine Shock, *J. Physiol.* **52** 355, 1918-1919.

4 Bodansky, M. Plasma Proteins in Experimental Anhydremia, *Proc. Soc. Biol. Chemists*, twentieth meeting, *J. Biol. Chem.* **67** 38, 1926.

5 Gasser, H. S., Erlanger, J., and Meek, W. J. Studies in Secondary Traumatic Shock. IV. The Blood Volume Changes and the Effect of Gum Acacia on Their Development, *Am. J. Physiol.* **50** 31, 1919-1920.

6 Bayliss, W. M. The Action of Gum Acacia on the Circulation, *J. Pharmacol. & Exper. Therap.* **15** 29, 1920-1921.

diffused through the capillary walls in shock, the concentration will become equal on both sides, and there is no longer any force resisting filtration or causing absorption

The toxemia of burns is particularly adaptable to the study of capillary permeability, because the symptoms persist for a number of days after the initial anhydremia has been replaced by a more normal fluid balance. This complicating factor has prevented extensive investigation of the problem in traumatic toxemia.

METHODS

The burns were treated by coagulation of the devitalized tissue with tannic acid,⁷ and were thereafter kept exposed to air. Fluids were forced energetically in an effort to restore fluid balance promptly.⁸ The patients were placed on a constant diet which consisted of approximately 60 Gm of protein and sufficient fat and carbohydrate to give a total value of about 2,500 calories. Food has little effect on the plasma proteins,⁹ but there are transitory changes following the ingestion of water. To insure uniformity, all samples of blood were taken before breakfast. The specimens were collected into test tubes containing powdered potassium oxalate. Generally, 20 cc of blood were withdrawn, and care was exerted to minimize venous stasis. The whole blood was then centrifugalized for twenty minutes at 2,500 revolutions per minute, and the volume of plasma was determined. The plasma was then pipetted from the cells, and duplicate analyses were made by the method of Wu.¹⁰

RESULTS

Total Plasma Proteins—The table gives the results of analyses of blood in ten patients with severe burns. The average total plasma proteins for the group at the expiration of twenty-four hours was 7.03 per cent, while the average volume of plasma was 59.1 per cent (chart 1). These values are considerably lower than those found by Plass and Matthew¹¹ in normal, nonpregnant women. During the next twenty-four hours the average for the group rose to 7.16 per cent, while the average volume of plasma (chart 2) was slightly lowered to 58.3 per

7 Davidson, E. C. Tannic Acid in the Treatment of Burns, *Surg Gynec Obst* **41** 202, 1925.

8 Underhill, F. P., Carrington, G. L., Kapsinow, R., and Pack, G. T. Blood Concentration Changes in Extensive Superficial Burns and Their Significance for Systemic Treatment, *Arch Int Med* **32** 31 (July) 1923.

9 Hanson, S., and McQuarrie, I. The Non-Dependence of the Protein Quotient in the Blood-Serum Upon the Rapidity of Metabolism with Especial Reference to the Non-Effect of Antipyretics, Sodium Cacodylate and Thyroid Extract, *J Pharmacol & Exper Therap* **10** 261, 1917.

10 Wu, H. A New Colorimetric Method for the Determination of Plasma Proteins *J Biol Chem* **51** 33, 1922.

11 Plass, E. D., and Matthew, C. W. Placental Transmission. IV. The Protein Fractions in Fetal and Maternal Plasma, *Am J Obst & Gynec* **12** 847, 1926.

Plasma Proteins Following Burns

Case	Date	Plasma Volume, per Cent	Fibrin, per Cent	Albumin, per Cent	Globulin, per Cent	Total Protein, per Cent
1	3/21	50.7	0.25	4.68		
	3/25	46.0	0.46	4.74	2.78	7.98
	3/26	55.3	0.53	4.04	2.14	6.71
	3/27	56.5	0.56	3.90	2.19	6.65
	3/28	55.9	0.73	4.45	2.52	7.70
	3/29	61.9	0.55	4.00	2.34	6.89
	3/30	55.7	0.56	4.51	2.67	7.74
	3/31	58.2	0.52	3.99	2.42	6.93
	4/ 1	53.6	0.50	4.48	2.52	7.50
	4/ 2	57.3	0.36	4.53	2.52	7.41
	4/ 3	54.0	0.47	4.70	2.67	7.84
2	5/17	55.5	0.46	4.42	2.42	7.30
	5/18	59.1	0.55	4.30	2.52	7.37
	5/19	61.2	0.56	4.08	2.09	6.73
	5/20	62.4	0.55	4.00	2.11	6.66
	5/21	62.5	0.50	4.20	2.30	7.00
	5/22	63.5	0.56	3.45	2.44	6.45
	5/23	63.1	0.47	3.97	2.77	7.21
	5/24	61.5	0.45	3.95	2.07	6.47
	5/25	62.5	0.46	3.67	2.39	6.52
	5/26	62.8	0.42	4.17	1.97	6.56
3	5/19	60.2	0.39	4.46	2.55	7.40
	5/20	62.6	0.42	4.20	2.14	6.76
	5/21	61.3	0.44	4.19	2.14	6.77
	5/22	61.3	0.66	4.13	2.75	7.54
	5/23	63.2	0.47	4.64	2.37	7.48
	5/24	62.6	0.41	4.25	2.07	6.73
	5/25	62.4	0.45	4.20	2.21	6.89
	5/26	61.2	0.45	4.96	2.04	7.45
4	6/ 7	67.2	0.41	4.36	2.64	7.41
	6/ 8	63.7	0.44	4.33	2.52	7.29
	6/ 9	68.0	0.45	4.03	2.53	7.01
	6/10	66.7	0.45	4.15	2.53	7.13
	6/11	61.2	0.45	4.23	2.66	7.34
	6/12	57.7	0.40	4.30	2.65	7.35
	6/14	65.6	0.50	4.61	3.12	8.23
	6/15	58.8	0.47	4.35	3.13	7.95
5	8/ 4	66.4	0.35	4.02	2.34	6.71
	8/ 5	61.4	0.50	4.03	3.10	7.63
	8/ 6	57.6	0.47	3.83	3.15	7.48
	8/ 7	59.0	0.49	4.07	3.12	7.68
	8/ 9	60.2	0.46	4.05	3.06	7.57
	8/10	63.2	0.45	4.09	2.96	7.50
	8/11	55.2	0.43	4.00	2.93	7.41
	8/12	59.0	0.45	4.10	2.75	7.30
	8/13	56.4	0.48	4.20	2.70	7.38
6	8/ 5	60.3	0.41	4.71	2.85	7.97
	8/ 6	63.4	0.41	3.99	2.55	6.95
	8/ 7	59.5	0.53	4.02	2.86	7.41
	8/ 9	61.8	0.64	4.31	2.61	7.56
	8/10	62.7	0.73	4.23	2.54	7.53
	8/11	59.1	0.83	4.52	2.17	7.52
	8/13	61.9	0.71	4.32	2.32	7.35
7	9/ 4	40.0	0.57	4.07	2.62	7.23
	9/ 5	55.5	0.65	2.95	2.65	6.26
	9/ 6	62.3	1.10	3.07	2.52	6.69
	9/ 7	63.0	1.25	3.35	2.35	6.95
	9/ 8	61.3	1.46	3.38	2.17	7.01
	9/ 9	59.5	1.38	3.32	2.25	6.95
	9/10	61.4	1.20	3.80	2.10	7.10
	9/11	62.3	0.95	4.00	2.11	7.10
	9/13	63.8	0.86	3.98	2.16	7.00
	9/14	64.0	0.75	4.30	2.20	7.25
8	6/10	63.0	0.26	4.06	1.94	6.26
	6/20	59.0	0.40	4.30	2.10	6.80
9	6/ 5	59.5	0.40	4.20	1.82	6.49
	6/15	60.1	0.41	4.20	2.08	6.69
10	6/10	64.4	0.38	4.50	2.12	7.00
	6/20	65.6	0.39	4.35	2.27	7.01

shows the most transitory fluctuations in concentration of any of the plasma proteins. This increased fibrin content of the plasma in patients suffering from burns is similar to that described by Foster and Whipple¹³ in a number of conditions in which there was injury and inflammation of tissue.

Globulin—The table gives the values obtained in analyses for the globulin content. The average for the group at the end of the first twenty-four hours was 2.30 per cent. This amount is somewhat lower than the average 2.69 per cent given by Plass and Matthew for normal, nonpregnant women. A subsequent rise of the globulin content was

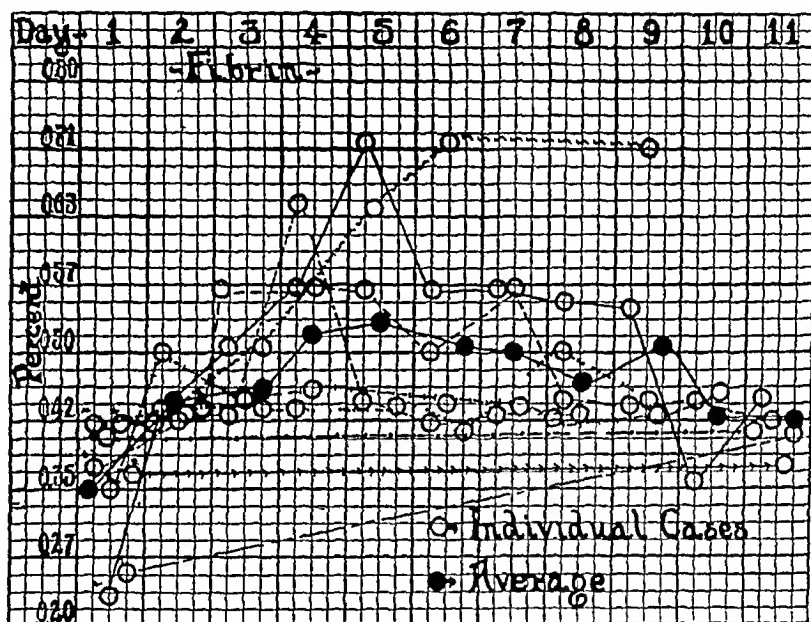


Chart 4—Fibrin content in individual cases and the average curve for the group. The rise is striking.

noted (chart 5), but this elevation did not reach the normal value. This slight rise is in accord with the observation of Rowe¹⁴ that there is a definite increase in the globulin content of the plasma in most conditions in which infection is present. The fact that the globulin did not change more strikingly under the stimulus of infection and injury may be due to the fact that there was a large initial loss of plasma, and the true extent of the loss was masked by the stimulus to formation of globulin by the burn.

13 Foster, D. P., and Whipple, G. H. Blood Fibrin Studies. IV. Fibrin Values Influenced by Cell Injury, Inflammation, Intoxication, Liver Injury and the Eck Fistula, *Am J Physiol* 58:407, 1921-1922.

14 Rowe, A. H. The Albumin and Globulin Content of Human Blood Serum, *Arch Int Med* 18:455 (Oct) 1916.

Albumin—The results of the albumin analyses are shown in the table. The alterations in the albumin content of the plasma in the extensive burns were uniform and were as characteristic as the changes noted for fibrin. The average value at the end of twenty-four hours for the group was 4.34 per cent, which is slightly lower than the average normal value of 4.45 per cent given by Howe.² A progressive lowering of the plasma albumin was observed for three days in the curve of the average for the series (chart 6). This was followed by a gradual elevation to normal. In case 7, in which there was the most extensive burn of the series, the depression in the value of the plasma albumin was striking,

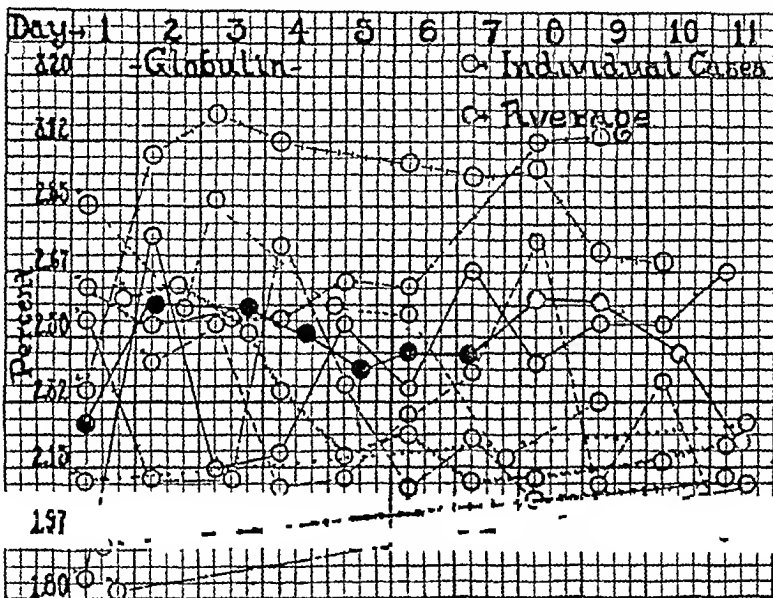


Chart 5—Globulin content in individual cases and the average curve for the group

and persisted for ten days. It is conceivable that in an extensive burn there may be a tremendous loss of plasma at the site of the burn, due to the effusion of the inflammatory exudate, and into the tissues in general from increased capillary permeability. Subsequently, when normal fluid balance becomes established dilution of the plasma occurs. A relatively slight difference is found in the total proteins because of the increase in fibrin and globulin content. On the other hand, albumin is regenerated more slowly than either fibrin or globulin,¹⁵ and, accordingly, the analyses show a persistent low value for albumin.

¹⁵ Kerr, W. J., Hurwitz, S. H. and Whipple, G. H. Regeneration of Blood Serum Proteins. I. Influence of Fasting Upon Curve of Protein Regeneration Following Plasma Depletion, *Am J Physiol* **47** 356, 1918-1919.

COMMENT

Under normal conditions the composition of the plasma is relatively constant, except for the changes in the fibrin content. According to Howe,² the concentration of the proteins varies with age, sex, feeding, physiologic activity, disease and reaction to infection. The changes in endothelial permeability in histamine and traumatic shock indicate possibilities of at least temporary modification in the concentration of proteins through such action.

Age and sex do not need to be considered variable in the present cases, because all of the patients were young men. The effect of diet is known to be of little consequence, but the precaution was taken to

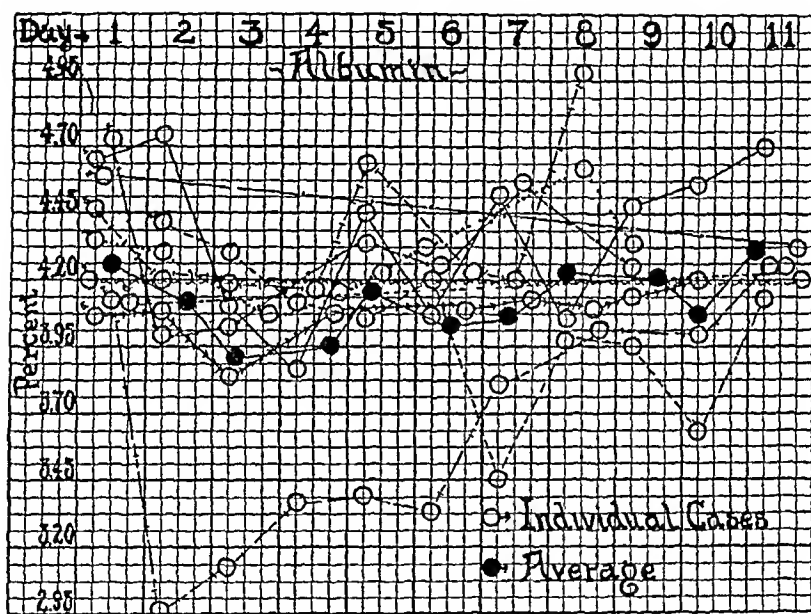


Chart 6—Albumin content in the individual cases and the average for the group. There is a marked depression of the albumin content.

obtain samples of blood before food was ingested. The activity of the patients was uniform, because the severity of the burns necessitated hospitalization.

The chief variable was the extent and severity of the burn. For instance, in case 7, in which approximately 50 per cent of the total surface of the body was burned, the changes are striking (chart 3), while in the less extensive burns only slight alterations were noted. In this instance, the red blood cell count rose to 7,270,000, and the volume of plasma was 40 per cent eighteen hours after the accident, but the total plasma proteins were only 7.26 per cent. The blood sugar at this time was 176 mg per hundred cubic centimeters. The fact that the value of the plasma proteins did not rise parallel to the degree of concentration of blood can be explained only on the basis of altered per-

meability of the capillary walls. The analysis showed that whole plasma was lost, rather than simply the water content.

The question may be raised whether the altered permeability involves all the capillaries of the body or only those employed in the process of forming the inflammatory exudate at the site of the burn. Hartman¹⁶ has demonstrated that there is an increased amount of epinephrine in the circulation after extensive burns. It has been shown further by Petersen, Levinson and Hughes¹⁷ that epinephrine increases endothelial permeability, and later lessens it. It would seem that concentration of the blood may be best explained on the basis of loss of plasma throughout the capillary bed of the body, as in traumatic shock, rather than on the basis of loss of fluid at the site of the lesion.

The changes just mentioned occurred primarily during the first twenty-four hours. The subsequent alterations noted may be best explained as phenomena of dilution.

CONCLUSIONS

1 In extensive burns there is first an increased permeability of the capillaries, which explains the characteristic concentration of blood in such cases.

2 There is no evidence to suggest that this alteration in the capillary walls persists during the period of toxemia. The late changes in the plasma proteins are probably phenomena of dilution.

3 The plasma fibrin and globulin show a characteristic rise, and the albumin shows a fall in concentration in burns.

REPORT OF CASES

CASE 1—E. F., a white man, aged 18, was admitted to the hospital on March 23, 1926, for treatment of burns which resulted from an explosion of oxygen. There were second degree burns of both hands and forearms. The face, ears and neck were burned to the second degree.

CASE 2—C. S., a white man, aged 33, was admitted to the hospital on May 15, 1926, for treatment of burns which resulted from an explosion of gasoline. There were second degree burns of the face, neck and hands.

CASE 3—H. G., a white man, aged 39, was admitted to the hospital on May 18, 1926, for treatment of burns which resulted from an explosion of gas. There were second degree burns of the entire face, neck and both forearms.

CASE 4—K. S., a white man, aged 30, was admitted to the hospital on June 5, 1926, for treatment of burns which resulted from an explosion of tar. There were second degree burns of the face, neck, left hand and forearm.

16 Hartman, F. A., Rose, W. J., and Smith, E. P. Influence of Burns on Epinephrin Secretion, *Am J Physiol* **78** 47, 1926.

17 Petersen, W. F., Levinson, S. A., and Hughes, T. P. Studies in Endothelial Permeability. I. The Effect of Epinephrin on Endothelial Permeability, *J Immunol* **8** 323, 1923.

CASE 5—O P, a white man, aged 22, was admitted to the hospital on Aug 3, 1926, for treatment of a burn from gasoline. There were second and third degree burns on the left side of the chest and the left flank, extending from the seventh rib to the crest of the ilium. The burned area began at the midline posteriorly and crossed the midline anteriorly. This area was surrounded by a margin about 5 inches (12.7 cm) wide which was burned to the first degree.

CASE 6—W R, a white man, was admitted to the hospital on Aug 4, 1926, for treatment of burns which resulted from an explosion of gas. There were second degree burns of the left arm, hand and face.

CASE 7—Z T, a white man, aged 25, was admitted to the hospital on Sept 3, 1926, for treatment of burns received when his clothes became ignited. There were third degree burns of the right side of the neck, and on the upper right forearm to the shoulder, involving the anterior, posterior and lateral surface. This extended into the axilla and then downward over the chest to the sixth rib. There were third degree burns of the left leg extending from the ankle to the knee. There was a similar third degree burn of the right leg. The remaining skin of both legs, from the toes up over the buttocks and involving the scrotum and perineum, was burned to the second degree. There were third degree burns over the sacral region and lower part of the back. There were also second degree burns of the left hand and arm. The cutaneous area involved was approximately 50 per cent of the total surface of the body.

CASE 8—W H, a white man, aged 22, was admitted to the hospital on July 15, 1926, for treatment of burns which resulted from an explosion of gasoline. There was a third degree burn involving the entire posterior aspect of the lower part of the left leg. The anterior and lateral aspects of the leg were burned to the second degree.

CASE 9—W C, a white man, aged 29, was admitted to the hospital on July 9, 1926, for treatment of burns which resulted from an explosion of gasoline. The entire right hand revealed a second degree burn. There was also a second degree burn of the lateral aspect of the right leg which involved about forty square inches.

CASE 10—A Y, a white man, aged 32, was admitted to the hospital on July 9, 1926, for treatment of burns which resulted from an explosion of gasoline. The entire left hand and the anterior aspect of the left leg were burned to the second degree.

THE CAROTID VENOUS PLEXUS AS THE PATH OF INFECTION IN THROMBOPHLEBITIS OF THE CAVERNOUS SINUS

ITS RELATION TO RETROPHARYNGEAL AND SPHENOIDAL SUPPURATION *

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SYNOPSIS

This communication is primarily to call attention to (1) a type of cavernous sinus thrombophlebitis of otitic origin, which, although far from uncommon, has not received due consideration, how diagnosed, and what surgical steps may be taken for its relief, for successful surgery depends on early diagnosis, (2) the part (a) an associated sphenoidal sinus suppuration or (b) nasopharyngeal abscess plays in the production and diagnosis of a thrombophlebitis of the cavernous sinus of otitic or jugular vein origin

Cavernous sinus thrombophlebitis of otitic origin is relatively not infrequent Brunner¹ records that in twenty-two autopsies performed on patients who had died from generalized aural sepsis (in whom cavernous sinus disease was not suspected) twelve showed a septic clot in the cavernous sinus, the route of invasion of two of the twelve being by way of the carotid venous plexus (as demonstrated microscopically) I have personally treated thirty-two patients suffering from cavernous sinus infection (there were six recoveries, five of which were operative and one spontaneous) Fifteen complete autopsies were made, in six of which the infection had originated from aural suppuration, and an additional patient, although the infection was of pterygomaxillary fossa origin, had a suppurative otitis prior to death (case 2)

The schematic drawing (fig 1) depicts the intracranial portion of the internal carotid artery (*I C A*) and the plexus of veins surrounding it (the carotid venous plexus) The latter communicates with the jugular bulb posteriorly (*d*) Anteriorly the plexus communicates with the cavernous sinus, the ophthalmics (*Op V*) and the small veins which pass through the foramen lacerum and foramen ovale from the pterygomaxillary fossa (*a*) All unite to form a "venous lake" at the anterior extremity of the cavernous sinus The chart also emphasizes

* Presented in part at the Fifty-Ninth Annual Meeting of the American Otological Society at Montreal, Canada, June 3, 1926

1 Brunner, H Contribution to the Knowledge of Otogenic Cavernous Phlebitis, *Monatschr f Ohrenh* 60 2, 1926

the communication of the carotid venous plexus with (b) the pharyngeal vault, and (c) the tympanic cavity, as well as the anterior venous communications of the cavernous sinus, and the ophthalmic with the veins of the pharynx, and their relationship to the retropharyngeal spaces, the pterygomaxillary fossa and the sphenoidal sinus mucous membrane²

ROUTES OF INVASION OF CAVERNOUS SINUS FROM AURAL SUPPURATION

There are two routes by which cavernous sinus thrombophlebitis of otitic origin may arise

(A) *Posterior (Petrosal) Involvement of the Cavernous Sinus*—Middle ear infection usually extends from the jugular bulb through

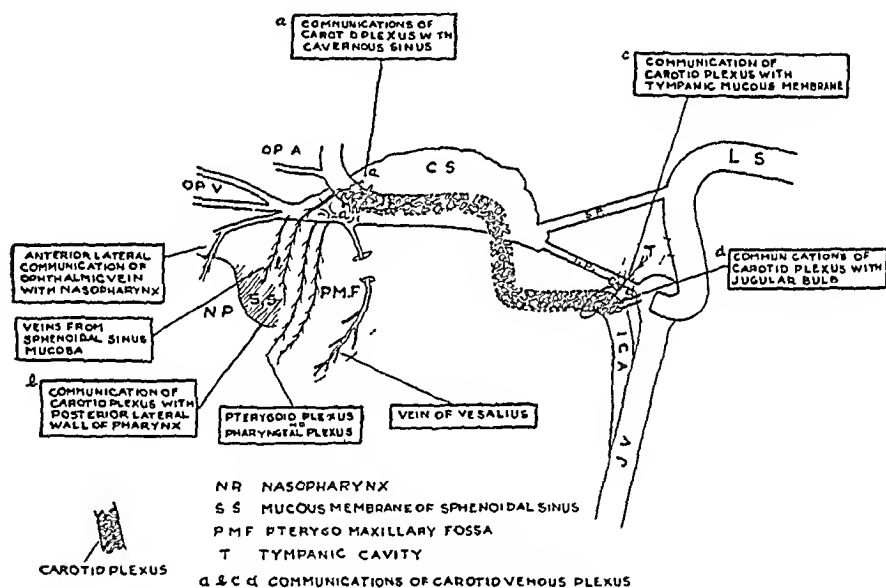


Fig 1—Schematic drawing of the communications of the carotid venous plexus

the inferior petrosal to the cavernous sinus, much less frequently, from the knee of the sigmoid by the superior petrosal. This group of cases is fairly well recognized.

With a petrosal sinus origin, the clot forms in the posterior portion of the cavernous sinus, from which it extends forward. Thus time is given for a readjustment of the venous circulation from the orbit prior to the involvement of the anterior extremity of the cavernous sinus, consequently, exophthalmos or chemosis is not produced, at least, not until an ophthalmic vein becomes occluded—which is generally in the

² Piebrantoni L. Vascular Relations Between Pharyngeal Vault and the Cranial Cavity, Arch ital d otol 36 626, 1925

terminal stage. It is the absence of early exophthalmos and chemosis which is responsible for the frequent failures to diagnose cavernous sinus suppuration in aural cases.

Clinical Diagnosis of Petrosal Cases When the infection passes through a petrosal sinus, symptoms referable to one or the other of the branches of the fifth nerve—such as pain behind the eye or in the teeth—may be present. In many cases the patients' teeth have been removed for the relief of pain when, in reality, edema of the nerve from infection of the adjacent sinus was the cause of this pain (case 2).

External rectus palsy may be an early symptom, the result of compression of the sixth nerve by the inflamed petrosal sinus as it passes under the sphenopetrous ligament. The third or fourth nerves or both may also be paralyzed by infiltration from the cavernous sinus during their course through it.

In chronic cases, exophthalmos, when it occurs at all, is likely to be a late manifestation due to the extension of the suppurative process into one of the ophthalmics, or the result of an orbital abscess. If, however, the phlebitis is fulminating, early chemosis and exophthalmos from venous occlusion may occur, but in the chronic pyemic cases, with great remissions of temperature and gradual clot formation, chemosis and exophthalmos do not occur.

(*B*) *Anterior (Carotid Plexus) Cases*—The second route by which an otitic suppuration may reach the cavernous sinus is through the small venous plexus which surrounds the carotid artery. In this type, the infection ascends through the carotid canal, and, as the carotid plexus communicates with the anterior portion of the cavernous sinus, chemosis and exophthalmos are usually early, though transient, symptoms.

Clinical Types of Carotid Plexus Cases Clinically, there are two types of carotid plexus invasion of the cavernous sinus of otitic origin: (1) cases associated with chronic aural suppuration, in which the thrombophlebitis of the plexus is secondary to caries of the bony covering of the carotid canal, situated in the anterior quadrant of the middle ear, which forms the posterior wall of the eustachian tube,³ (2) cases which follow an acute aural suppuration, the phlebitis reaching the carotid plexus either by (*a*) a dehiscence in the floor of the tympanic cavity, (*b*) an osteophlebitis of a tympanic communication of the carotid plexus, or (*c*) secondary to a jugular bulb phlebitis.

Having once involved the small plexus surrounding the carotid artery the phlebitic process is more likely to be transmitted to the cavernous sinus, because of the pulsating movement of the artery.

Another anatomic peculiarity is that infection by the carotid plexus attacks the cavernous sinus at its anterior extremity through the "venous

³ Alexander, G. Orogenic Thrombophlebitis of the Cavernous Sinus. *Monatschr f Ohrenh* 59 971 1925.

lake," which is made up of the ophthalmics, the veins from the nasopharynx and pterygomaxillary fossa, and the carotid plexus (*a* and *b* of scheme) Partial occlusion of the anterior end of the cavernous sinus, which causes a sudden associated disturbance of the return circulation, gives rise to slight exophthalmos and chemosis at an early stage in the disease However, as the venous communications of the orbit are free, the proptosis and chemosis rapidly disappear with the reestablishment of the venous return Later, there may be a recurrence of the exophthalmos and chemosis from a forward extension of the thrombophlebitis in the ophthalmics, with or without an orbital abscess

Diagnosis of Carotid Plexus Cases (*a*) A suppurating ear associated with signs of acute sepsis and slight chemosis and exophthalmos should suggest that the cavernous sinus has been infected by way of the carotid plexus

(*b*) A chronic otitic sepsis (slight rise in temperature and sweating, or severe remissions) associated with the operative findings of caries and granulations in the anterior quadrant of the tympanic cavity during operation makes a thrombophlebitis of the carotid plexus a possible diagnosis

Granulations on the carotid artery, disclosed during a radical operation performed for the cure of suppuration alone (unassociated with signs of sepsis), should not be curetted The trauma of their removal was followed by a carotid plexus thrombophlebitis in one of my early cases

RELATION OF RETROPHARYNGEAL SUPPURATION TO DISEASE OF THE CAVERNOUS SINUS

The significance of a retropharyngeal abscess in the diagnosis of cavernous sinus thrombophlebitis in the presence of aural suppuration *after infancy* has not been sufficiently emphasized, although an examination of the literature disclosed a considerable number of cases The postpharyngeal suppuration originates from retrograde thrombophlebitis of the veins communicating with the cavernous sinus and the pharynx, and is likely to pass unrecognized, because its location in the lateral wall of the superior portion of the nasopharynx—that is, above the palate—prevents the swelling from being seen during oral examination Consequently, (*c*) a retropharyngeal or a pterygomaxillary fossa abscess in the course of an aural sepsis in a patient over 18 months of age should suggest that the cavernous sinus is involved

CASE 1—*Acute otitic pyemic sepsis with early involvement of the cavernous sinus by the carotid plexus associated with a secondary pterygomaxillary fossa abscess*⁴

4 Detailed history in Eagleton, W P Cavernous Sinus Thrombophlebitis and Allied Septic and Traumatic Lesions of the Basal Venous Sinuses, The Macmillan Company, 1926, French translation, Masson et Cie

The accompanying temperature chart resembles the excursions of lateral sinus thrombosis (fig 2)

History—A boy, aged 6, had had an earache, followed by delirium and a chill. A paracentesis was performed. From an early stage of the condition the pulse rate was disproportionately accelerated (showing profound intoxication). On the seventh day of the disease the mastoid was explored, little pathologic change was found. The day after the operation the child had slight exophthalmos with chemosis, which had disappeared on the following day. (Although their diagnostic significance was not appreciated, the exophthalmos and chemosis were indicative that the infection had passed through a dehiscence in the floor of the tympanum into the jugular bulb, and ascending through the carotid plexus had involved the cavernous sinus as in no other way could a proptosis be produced as early as the eighth day after the original earache.)

The temperature continued to be pyemic, but the patient did not have chills. Blood cultures were negative throughout. The lateral sinus was explored, but no clot or phlebitis was demonstrated.

On the sixteenth day the child had a *recurrence of the exophthalmos* with slight external ocular paralysis—ptosis and double vision. A diagnosis of "cavernous sinus thrombosis from jugular bulb phlebitis" was then made.

The carotid artery was ligated and the jugular bulb opened; the latter contained free pus. *The exophthalmos and chemosis immediately disappeared and did not recur*, although the child lived for several weeks.

A second chill occurred on the twentieth day of the disease. On the twenty-fifth day the patient developed *difficulty in swallowing, but did not complain of pain. Nothing could be seen in the throat, but a soft mass could be felt in the upper posterior lateral angle of the nasopharynx* (to which little attention was paid because of the absence of pain and the difficulty in breathing).

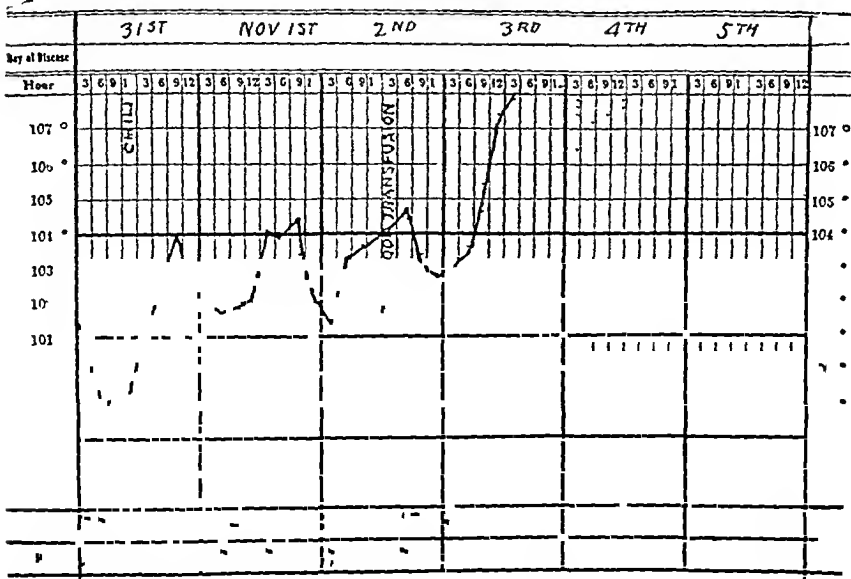
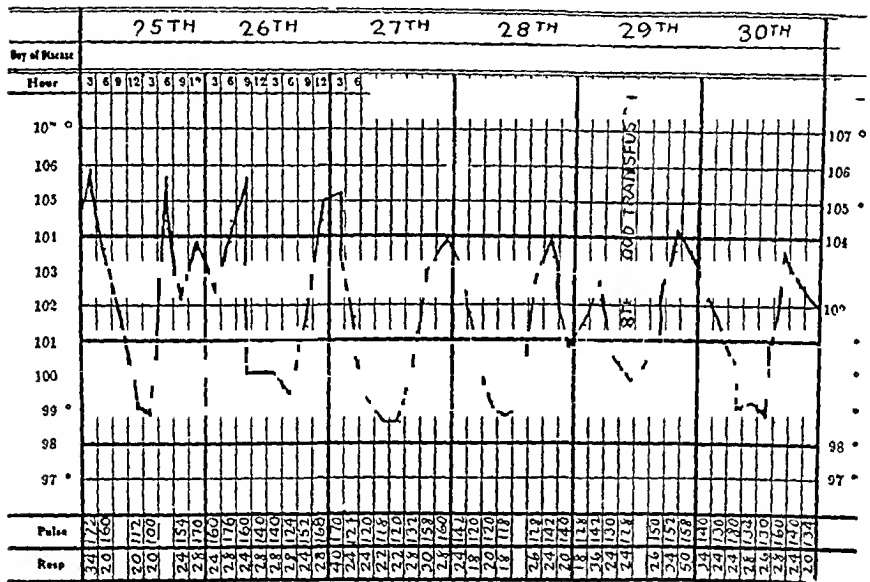
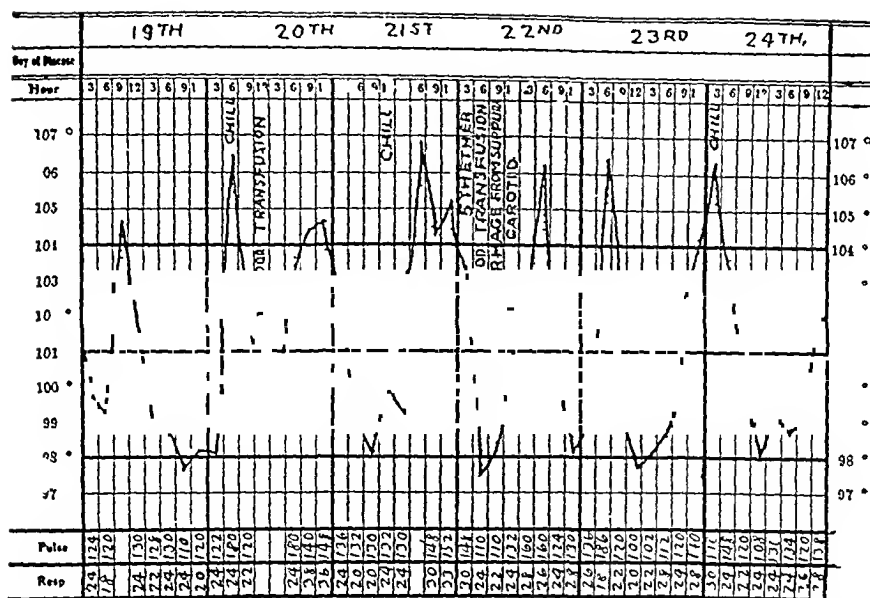
Death occurred from a terminal meningitis.

Autopsy (Dr John V Bissett)—The petrosal sinuses were normal, and the infection in the jugular bulb had been controlled by drainage. The upper end of the carotid canal and the cavernous sinus of the homolateral side were bathed in free pus. The infection also involved the opposite cavernous sinus. The superior portion of the nasopharynx contained an abscess beneath the mucous membrane which filled the pterygomaxillary fossa, the upper boundary of the abscess was formed by the base of the skull, with the foramen lacerum as its center. The abscess apparently had developed from a thrombophlebitis of the veins passing from the cavernous sinus into the nasopharynx through the lacerum. *The sphenoidal sinus contained free pus.*

INFLUENCE OF CHRONIC SPHENOIDAL SUPPURATION IN CAUSATION OF DISEASE OF THE CAVERNOUS SINUS

A *previous*, though quiescent, infection of the sphenoidal mucous membrane may be a causative factor in the production of septic phlebitis of the cavernous sinus when there is superadded another infection—acute otitis media, tonsillitis, or sinusitis—or severe trauma from operative procedure (such as enucleation of tonsils or sphenoidal sinus exenteration). This has not hitherto been emphasized, although O'Malley⁵ observed that in all cases of death from disease of the

⁵ In discussion of paper by Davis, H. J. Proc. Roy. Soc. Med. 1912.



f aural origin, with transient exophthalmos and chemosis (case 1)

cavernous sinus following a tonsillectomy the sphenoid had been involved

On the other hand, Turner and Reynolds⁶ have demonstrated microscopically that the sphenoidal suppuration which accompanies cavernous sinus disease (as in the case herein reported) is secondary to the infection of the cavernous sinus, the sphenoidal suppuration being due to nutritional death of (submucous, and osseous) tissue the result of a thrombophlebitis which descends from the cavernous sinus into the sphenoid

An existing but quiescent inflammation of the sphenoid may be a causative factor in the production of a cavernous sinus infection because (1) The sphenoid is the only accessory sinus in anatomic proximity to a large venous radicle in which the circulation is free, but slow, with many eddies, this is favorable to the production of a septic thrombophlebitis (2) In suppuration of the sphenoidal mucosa, the infection is separated from the cavernous sinus by a thin layer of compact bone especially liable to nutritional death from circulatory disturbance (I have found "discoloration and roughness of the intracranial surface of the sphenoid" to be a usual postmortem condition in cavernous sinus infection) (3) The sphenoid is lined with a delicate mucous membrane (normally easily detached from the bone) (4) Finally, both the mucous membrane and bone are perforated by veins (the sphenoidal plexus) which empty into the cavernous sinus Consequently, when a sphenoidal sinus is the seat of a chronic purulent inflammation, accompanied as it must be by thrombosis of many of its small veins, and later is attacked by an acute intercurrent infection, its veins are especially likely to become the avenue of an infection to the cavernous sinus, since the superimposed acute phlebitic process passes through only a few millimeters of thrombosed tissue before it enters directly into the large venous radicle

The cavernous sinus, because of its relationship to the veins of the sphenoid sinus, lacks the protection afforded to infection from the pterygoid and pharyngeal plexus—a long course through dense mucous and submucous tissue muscle, fascia and bone of the pharyngeal vault and base of the skull The anterior extremity of the cavernous sinus thus possesses anatomic and physiologic factors favorable to the intracranial extension of venous infection which are not found in any other region of the head

Influence of Trauma—If such be the fact, it is evident that (1) all unnecessary operative trauma should be avoided (at least for a considerable period) whenever the history warrants the suspicion that a previous

⁶ Turner, A, Logan and Reynolds, F Esmond Furuncle of the Right Nasal Vestibular Septic Thrombosis of the Cavernous Blood Sinuses, Leptomeningitis Death Autopsy J Laryng & Otol 41 73 (Feb) 1926

sphenoidal sinus infection was associated with an osteophlebitis of the sphenoidal vein—pain on top of the head or behind the eyes, and blurred vision accompanied by a persistent nasopharyngeal discharge

(2) An associated suppurative process—acute otitis media, tonsillitis or sinusitis—should be regarded with apprehension if accompanied by the slightest symptoms of cavernous sinus disease

CASE 2—*Chronic infection of the pterygomaxillary fossa (of dental origin) ascended as a thrombophlebitis and entered the cranium by the foramen ovale, giving rise to (1) pus in both cavernous sinuses, (2) extradural abscess, (3) localized meningitis of the floor of the middle fossa and (4) a brain abscess in the anterior portion of the temporosphenoidal lobe. Later, the phlebotic process retrograded through the carotid plexus and occasioned (5) a jugular bulb and sigmoid sinus suppuration and finally (6) a purulent otitis and mastoiditis, the latter probably occurring from an osteophlebitis of the veins of the floor of the middle ear and mastoid*

Previous History—About nine months before he was admitted to the hospital, the patient, a man, noticed that the skin on his face and body was becoming yellow. This condition was accompanied by a feeling of general weakness. One week later, he suffered from pain in his teeth and a slight swelling of the right side of his face. Two upper back teeth were removed. Following the extraction he could not open his jaw. He remained in bed for two weeks. Later, the jaw was cured. In spite of continued dental treatment, he gradually grew weaker. The swelling of the face subsided somewhat, but he began to have pain in his lower teeth, this was relieved by an extraction. During the next month, although able to work, he consulted several physicians because of the swelling and pain over the right side of the upper jaw. One physician diagnosed the condition as "gumma of the jaw." In February, seven months after the beginning of his illness and two months before admission to the hospital, the patient was hit on the swollen part of the jaw. From this time, the pain, edema and illness increased.

On April 20, he was admitted to the Newark City Hospital. He was conscious but "dopy," complained of pain in the jaw and dizziness, and had the low, irregular temperature of chronic sepsis.

Examination—The right side of the face and eye were swollen. The swelling resembled that of an abscess under the temporal muscle, however, it had a sharp line of demarcation as if the pressure was under the parotid gland rather than under the temporal muscle. It did not extend downward into the neck or involve the lower jaw. The edema of the lids of the right eye was so great that the eye could not be seen, but forcible retraction showed that there was no proptosis. The mouth could not be opened.

The blood count showed red cells, 4,800,000, leukocytes, 13,000, polymorphonuclears, 75 per cent, lymphocytes, 25 per cent. Repeated blood cultures were negative.

Diagnosis—The condition was diagnosed as "pterygomaxillary-fossa infection subsequent to infiltration of the dental canal from the extraction of teeth, with acute exacerbation developing seven months later from trauma followed by an osteomyelitis and a protective meningitis of the floor of the middle fossa from an ascending thrombophlebitis." (The diagnosis was based on (1) the history, (2) the limitation of the swelling, (3) the inability to open the jaw, (4) the presence of chronic sepsis and (5) the mental state of the patient.)

Operation was advised. This was to consist of a "radical exploration of the pterygomaxillary fossa and base of skull, to be preceded by ligation of the carotid plexus and possibly associated with injury to the facial nerve, if the infective process in the bone could not otherwise be fully eliminated" (This major procedure was suggested because I had seen a patient with a similar chronic pterygomaxillary-fossa infection which seventeen skin incisions for the evacuation of pus had failed to control)

Subsequent History—The temperature continued to be irregular and slightly elevated. The patient complained of a constant pain in the face and the side of the head, but he became rational and alert. The swelling of the side of the head and face having extended upward into the temporal region, on May 6, a skin incision was made which evacuated a quantity of pus from under the temporal muscle. An incision below the angle of the jaw was performed on May 12, and another one was made on June 3, each time liberating a considerable amount of pus and followed by a marked subsidence of the swelling and relief from pain. The chronic septic condition continued, however, associated with a loss of flesh.

On June 10, he was unable to move his eye outward because of right external rectus paralysis (which may have been present for some time as previously the swelling of the lids prevented an inspection of the ocular movements).

The patient had complained of slight pain in the right ear, on June 13, there was profuse discharge with a perforated drum membrane.

On the morning of June 21, the patient was slightly dazed, but was able to answer all questions intelligently and promptly. Suddenly he had repeated convulsions, characterized by "nystagmus to the left, a spasticity of the left arm and leg, with complete flaccidity of the right arm and leg." A lumbar puncture was made, the fluid was clear and under moderate pressure, the number of cells had not increased and no organisms were found in the smear or on the culture.

(Following the convulsions he again became rational and alert.)

On June 25, it was decided that if the patient could be put into condition for an operation, the pterygomaxillary fossa should be entered (going across the base of the skull) and an effort made to combat what undoubtedly seemed to be a pterygomaxillary abscess, with secondary thrombophlebitis of the veins passing either through the foramen lacerum or ovale. The thrombophlebitis had occasioned an osteomyelitis of the base of the skull, with an extradural abscess, a localized meningitis or a brain abscess.

Death followed a blood transfusion prior to the operation.

Autopsy (Dr Harrison S Martland)—*Soft Parts* The reflection of the scalp revealed extensive edema of the right temporal muscle with pus, which came from below, between the muscle and bone.

Nasopharynx The inflammatory infiltration extended across the base of the skull into the pterygomaxillary fossa, internal to which on the posterior pharyngeal wall of the right side (between it and the anterior body of the vertebrae) there was a large amount of pus.

This condition existed, although the only difficulty in swallowing that the patient had was attributable to the injury and external swelling. The only complaint of dysphagia was recorded on June 6 in the nurses' record "*fluids taken fairly well but difficulty in swallowing*"

Bones of Base of Skull The base of the skull did not contain microscopic evidence of caries or necrosis. There was a purulent extradural exudate on

the inner half of the floor of the right middle fossa, which contained considerable pus, the center of the purulent area was over the fossa ovalis

Basal Sinuses The right and left cavernous sinuses contained free pus. There was a thin, purulent exudate on the subdural surface of the left middle fossa in the region of the cavernous sinus. There was purulent thrombophlebitis of the right jugular bulb, while the descending portion of the right sigmoid contained a clot. (The infection apparently entered by the veins of the ovale, involved the right cavernous sinus, and descended, by way of the carotid plexus, to the jugular bulb, as the petrosal sinuses were not infected.)

Meninges and Brain The removal of the brain revealed numerous adhesions of the tip of the right temporal sphenoidal lobe. The pia-arachnoid of this area was slightly brownish. The breaking of the adhesions revealed an abscess in the brain substance, the adhesions to the floor of the right middle fossa forming its stalk and walling it off from the rest of the meninges. The abscess cavity was from about $\frac{3}{4}$ to 1 inch (1.8 cm. to 2.5 cm.) in size and filled with greenish pus. It had a capsule, made up of a granulating membrane from 2 to 3 mm. thick and slightly red. The cavity of the abscess was situated below the ventricle and the caudate nucleus, and extended to within a few millimeters of the descending horn of the right lateral ventricle. The brain tissue surrounding the upper part of the abscess was slightly yellow and edematous, the edema encroached on the corpora striata. The right lateral ventricle was somewhat compressed in the middle. In the overlying ependyma there were small punctate hemorrhages.

Evidence of general meningitis was not found.

The right mastoid contained some pus (a recent process, as the cells were not broken down).

The sphenoidal cells were free.

Comment—From the history of the patient and the postmortem observations, it is evident that (1) the infection followed a therapeutic infiltration of a dental canal. After a prolonged period of activity it became semiquiescent but (2) underwent an acute exacerbation as the result of the trauma from a blow. From this time the patient suffered from (3) an abscess in the pterygomaxillary fossa associated with (4) thrombophlebitis.

The abscess (encased externally by the parotid gland and the fascia) dissected upward under the temporal muscle, downward into the neck, and forward into the cheek and was evacuated in all these regions, while the deeper pterygomaxillary collection (although causing trismus from infiltration of the pterygoid muscles) did not occasion difficulty in swallowing or interfere with respiration because of its high position.

The infective process was not controlled by the peripheral incisions because from the beginning it involved the venous radicles of the pterygomaxillary fossa, by them it entered the skull through the foramen ovale and invaded the right cavernous sinus, from the right it extended to the opposite cavernous sinus. The chief area of intravenous purulent accumulation was the lake at the anterior end of the right cavernous sinus, from it the thrombophlebitis traversed the carotid plexus to the jugular bulb, from which it retrograded into the sigmoid sinus.

A thrombophlebitis of one of the smaller radicles caused (1) the protective meningitis—as evinced by adhesions of the brain to the dura—and (2) the brain abscess with a capsule and stalk

A few days before the death of the patient the phlebitic process manifested itself by a suppurative otitis, probably from a thrombophlebitis of the veins entering from the jugular bulb or carotid plexus, as necrosis of the bone was not found at autopsy (This view is strengthened by the fact that a retropharyngeal abscess associated with mastoid involvement from direct extension through the base of the previous pyramid, although a not uncommon complication in infants by way of a dehiscence, is unknown in adults without microscopic evidence of necrosis or caries)

PRINCIPLES OF SURGICAL TREATMENT OF CAVERNOUS SINUS INFECTION

(a) When there is a reasonable suspicion of cavernous sinus infection, the inflamed sinus should be placed at rest by fractional⁷ or complete ligation of the internal carotid

(b) Following this, the large venous radicle into which the smaller vein empties, or through which the primary or secondary area of infection has been transmitted, must be surgically opened

(c) Nature's reparative processes must be aided—by repeated transfusions, preferably from an immunized donor

Treatment—Of chief importance is the early diagnosis that the infection *has probably reached the cavernous sinus*, but whether it ascended (a) by way of the petrosal sinuses (coming from behind, with symptoms of pain from involvement of the fifth nerve with ocular paralysis from the third and fourth nerve), or (b) by the carotid plexus (attacking the sinus from in front, thus causing transient exophthalmos) is of secondary consideration

(1) Aid to Spontaneous Recovery Although it is recognized that rest is necessary in nonpurulent phlebitic processes, the application of the principle in the treatment of septic phlebitis has not been sufficiently emphasized

My experience would suggest that if, during an early stage of cavernous sinus infection—before the clot has broken down—the inflamed parts are placed at rest, and the primary focus radically removed, spontaneous recovery will result in a considerable proportion of cases Rest of an inflamed cavernous sinus can be obtained only by stopping the pulsations of the intracranial portion of the internal carotid, as it is contained within the cavernous sinus For I am convinced that any trauma of a vein which is the seat of a septic process—

⁷ Kerr, H H Fractional Ligation of Common Carotid Artery in Treatment of Pulsating Exophthalmos, Surg Gynec Obst 41 565 (Nov) 1925

whether caused by injury during operation, forcible palpation during examination, movement from the contractions of adjacent muscles or the pulsations of an accompanying artery—not only tends to prevent Nature's control of the infection by clot formation, obliteration and canalization, but in the vast majority of cases is the deciding factor in the propagation and extension of the septic process itself

(2) Indications for Opening the Cavernous Sinus The foregoing cases and autopsies demonstrate that pus and broken-down clot usually are located only in the large venous sinuses, where the circulation is free but slow The smaller venous tracts, such as the petrosals, the veins of Vesalius, or the carotid plexus (while frequenting the route of a transmitting retrograde thrombophlebitis), are anatomically adapted to a spontaneous cure by obliteration Consequently, when there is clinical evidence that the cavernous sinus is the seat of a purulent collection—such as a continuation of pyemic sepsis after the jugular bulb has been opened, or when the infection has resulted from a retrograde thrombophlebitis from the nasopharynx (case 2)—the large venous lake itself should be opened

(3) Surgical Approach to Sinus The operative attack should follow the path of the infection as far as possible However, if there is extreme exophthalmos—and a blind eye—the sinus can be adequately drained from in front by Mosher's ⁸ operation, after the common carotid has been ligated The latter not only diminishes hemorrhage which is otherwise uncontrolled, but also puts the parts at rest

If the infection has passed a petrosal sinus, the cavernous sinus may be opened along the floor of the middle fossa All efforts to drain through the petrosals themselves (as advocated by Ballance ⁹) have been unsuccessful This is to be expected on anatomic and pathologic grounds, except possibly in the cases of a very large petrosal with free pus throughout its entire extent—a very rare condition

If the infection has ascended by the carotid plexus, early carotid ligation with an exploration of the jugular bulb should be followed by an incision of the cavernous sinus through the middle fossa

An associated *retropharyngeal* abscess may be drained through the mouth, but a *pharyngomaxillary* abscess must be evacuated externally

⁸ Mosher, Harris Peyton The Orbital Approach to the Cavernous Sinus, *Laryngoscope* 24 709-717, 1914

⁹ Ballance, C A, and Hobhouse, Neil A Case of Septic Thrombosis of the Left Sigmoid, Cavernous and Inferior Petrosal Sinuses a Suggestion for Treatment in Future Cases, Tr Ninth Internat Otol Congress, Boston, 1912

THE STATUS OF ENTEROSTOMY IN THE TREATMENT OF ACUTE ILEUS

A STATISTICAL INQUIRY *

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AND

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Any one who is interested in the treatment of patients with acute ileus must have been encouraged by the enthusiastic recommendation that has been given to enterostomy as a life-saving procedure. Within the past fifteen years, Elsberg,¹ Woolsey,² Bonney,³ McGlannan,⁴ McKenna,⁵ McKinnon,⁶ Richardson,⁷ Summers,⁸ DeLore and Conrozier,⁹ Wortman,¹⁰ Vollhardt,¹¹ Walker,¹² C H Mayo,¹³ Barber,¹⁴ Boit,¹⁵ W J Mayo,¹⁶ Taylor¹⁷ and many others have recommended the use of enterostomy, particularly of a high jejunostomy. Some of these observers have reported cases to support their recommendations, a few have reported series of cases, while others have merely enthusiastically recommended jejunostomy. Since some of these recommendations were authoritative, we were inclined to accept them, but certain facts have led us to question the procedure. For example, we found that there was a high mortality rate in the enterostomy group of a series of cases of

* Read before the Section on Surgery at the Annual Meeting of the Medical Society of the State of New York, May 13, 1925

- 1 Elsberg, C A Ann Surg **47** 737, 1908
- 2 Woolsey, George Surg Gynec Obst **10** 608, 1910
- 3 Bonney, Victor Arch Middlesex Hosp, 21, 1910, Brit M J **1** 583 1916
- 4 McGlannan, A Intestinal Obstruction, J A M A **60** 733 (Oct) 1913
- 5 McKenna, C H Surg Gynec Obst **17** 674, 1913
- 6 McKinnon, A I Medical Herald **36** 268 (Dec) 1917, Jejunostomy, J A M A **77** 273 (July 23) 1921
- 7 Richardson, E P Boston M & S J **183** 288 (Sept 2) 1920
- 8 Summers, J E Ann Surg **72** 201 (Aug) 1920, Surg Gynec Obst **32** 412 (May) 1921
- 9 DeLore and Conrozier Rev de chir **2** 605, 1920
- 10 Wortman, W Med Klin **17** 932 (July 31) 1921
- 11 Vollhardt, W Deutsche Ztschr f Chir **164** 352 (July) 1921
- 12 Walker, I J Boston M & S J **186** 108 (Jan 26) 1922
- 13 Mayo, C H Acute Intestinal Obstruction, J A M A **79** 194 (July 15) 1922
- 14 Barber, W H Enteroparesis, J A M A **79** 1824 (Nov 25) 1922
- 15 Boit, Hans Beitr klin Chir **125** 476, 1922
- 16 Mayo, W J Surg Gynec Obst **36** 447 (April) 1923
- 17 Taylor, Sir W Surg Gynec Obst **38** 270, 1924

acute ileus at the Presbyterian Hospital, from 1914 to 1923, inclusive. Moreover, the mortality rate in a similar group at the Roosevelt Hospital, from 1910 to 1919, inclusive, agreed closely with the results at the Presbyterian Hospital. We examined the recent literature on acute ileus and compiled as many statistics of case series as we could find, up to 1924. However, the actual statistics do not seem altogether to support the claims of those who have recommended enterostomy. We have not been able to discover definite, incontrovertible proof that enterostomy has lowered the mortality rate in cases of acute ileus.

The evidence furnished by any small group of patients on whom enterostomy had been performed is not of any definite value unless it concerns all of the patients in that particular series of cases of acute

TABLE 1—*Groups of Enterostomy Cases**

Date Published or Years Covered	Name of Author or Hospital Reporting	Number of Cases	Number of Deaths	Mortality Percentage
Published 1913 (1893-1912, inc.)	A. McGinnan Johns Hopkins Hospital St. Agnes Hospital	81	40	49.4
Published 1920	E. A. Codman	12	7	58.3
Published 1920 (1910-1919, inc.)	E. P. Richardson Massachusetts General Hospital	36	18	50.0
Unpublished (1910-1919, inc.)	The Roosevelt Hospital, New York City	47	37	78.7
Published 1921 (1911-1920, inc.)	J. M. T. Finney Johns Hopkins Hospital Union Memorial Hospital	48	29	60.4
Published 1921	W. Wortman	35	12	34.3
Unpublished (1914-1923, inc.)	The Presbyterian Hospital, New York City	90	69	76.6
Total		349	212	
Average mortality of collected cases				60.7

* These groups are isolated from the series collected in table 2.

ileus who received similar treatment. Even then, the evidence is inconclusive because of the great variations that occur in the mortality rate of small series. At the Presbyterian Hospital we found one group of eleven consecutive patients on whom enterostomy was performed in which the mortality rate was only 10 per cent, and another similar group with a mortality rate of 90 per cent. Nevertheless, we have included in our enterostomy table one small group because it appeared to be complete and was published as a part of a series by an observer of recognized conservatism. A comparison of tables 1 and 2 shows that the average mortality rate for patients with acute ileus on whom enterostomy is performed is 19 per cent higher than that for the entire series in the present compilation. Further comparison shows that in every series quoted, the mortality rate of the enterostomy group is higher than that of the series. A comparison of the mortality rate of the enterostomy group with that of the nonenterostomy group is even more striking and less favorable to enterostomy (table 3).

There must be some explanation for this disagreement between what appear to be the facts and what are believed to be the facts by a considerable number of competent observers. The basis for the belief that enterostomy is effective in the treatment of acute ileus is subjective, and therefore to be mistrusted. One fact is not compared with another fact, but rather a fact is compared with a supposition. The patient who is expected to die recovers after an enterostomy has been performed, and the enterostomy is believed to have been responsible for the recovery.

TABLE 2—*Series of Cases of Acute Ileus**

Date Published or Years Covered	Name of Author or Hospital Reporting	Number of Cases	Number of Deaths	Mortality Percentage
Published 1913 (1893-1912, inc)	A McGinnan Johns Hopkins Hospital St Agnes Hospital	181	73	40.3
Published 1920	E A Codman	41	14	34.1
Published 1920 (1908-1917, inc)	E P Richardson Massachusetts General Hospital	118	49	41.5
Unpublished (1910-1919, inc)	The Roosevelt Hospital, New York City	186	88	47.3
Published 1921 (1911-1920, inc)	J M T Finney Johns Hopkins Hospital Union Memorial Hospital	217	76	35.0
Published 1921	W Wortman	172	55	31.9
Unpublished (1914-1923, inc)	The Presbyterian Hospital, New York City	174	101	58.0
Total		1,089	456	
Average mortality of collected cases				41.8

* The enterostomy groups collected in table 1 are included in these series.

TABLE 3—*Comparison of Mortality in Acute Ileus Series Compiled in 1900 and in 1925**

Cases Referred to 1900 and 1925 Collections	1,000 cases compiled by C. D. Gibson, published in 1900		1,089 cases compiled by the present writers in 1925	
	Number of Cases		Mortality Percentage	
	1900 Series	1925 Series	1900 Series	1925 Series
Entire series	1,000	1,089	43.2	41.8
Nonenterostomy group	810	740	38.2	33.0
Enterostomy group	190	349	64.2	60.7

* The reduction in mortality of nonenterostomy group is slightly greater than in the enterostomy group.

The fact is that the patient lived, and the supposition is that he would have died. Perhaps we are prejudiced in favor of enterostomy, knowing that in controlled animal experiment, evacuation and irrigation of obstructed loops is of proved efficacy. On the other hand, certain cases of acute ileus in which the patient was expected to die and in which recovery was made without enterostomy, are likely to be forgotten. In bedside experiments there is no control except the painstaking honest comparison of carefully checked statistics. We believe that a certain amount of the enthusiasm for enterostomy in the treatment of acute ileus is a result of a natural optimism unchecked by careful reasoning.

and of a failure to test theory against experience, but we cannot believe that this is the complete explanation

If there is anything in our compilation of statistics to support the present enthusiasm for enterostomy, we have not discovered it. We had hoped to be able to show that enterostomy is an effective treatment, we are still inclined to believe that it is, but we find ourselves trying to explain why statistics do not show it.

At first one may be shocked to find the mortality rate of the enterostomy group of patients so much higher than that of the nonenterostomy group in the same series. In the series that Gibson collected, it was 26 per cent higher and in this series almost 28 per cent higher (table 3). In considering these statistics, enterostomy appears to be a dangerous

TABLE 4—*Rise in Mortality Rate Due to Late Operation*

Taken from the Roosevelt Hospital Statistics, 1910-1919, inclusive
Time between onset and operation was recorded in only 164 cases

Mortality Percentage	Hours Between Onset and Operation				
	12	24	48	72	72+
90					
80					
70					7 ^a
60					
50			32	20	
40					
30					
20		25			
10					
	28				

Average mortality of all cases was 49.7 per cent. Numbers represent the number of cases in which operation was performed in the 12 or 24 hour period.

procedure. It must be kept in mind, however, that enterostomy has not been performed as a routine procedure. It was performed only in 19 per cent of Gibson's compiled series and in 32 per cent of the present compiled series. This operation has been reserved generally for those cases in which the patient is sickest or the disease is most advanced, or both (table 5, star footnote).

It is fallacious to compare the mortality rate of the entire enterostomy group with that of the entire nonenterostomy group in any series until it is determined whether each comprises the same percentage of late cases as does the other. It is recognized generally that the mortality rate of patients with acute ileus depends primarily on the time at which operation is performed rather than on the type of operation (tables 4 and 9). The entire enterostomy group includes about the same percentage of late cases as the entire nonenterostomy group of our series at the Presbyterian Hospital (table 5 dagger footnote) and therefore (if other factors were equal), its mortality rate should be about the same. We have made a comparison of this enterostomy group with the nonenterostomy

group in table 6, and find that the mortality rate of the entire enterostomy group is considerably higher than that of the entire nonenterostomy group. The same fact has been noted in table 3 in which we compared the mortality of enterostomy and nonenterostomy groups having an unknown percentage of late cases. These observations tend to confirm each other. In table 7 we have compared the mortality of the late (72+ hour) groups of cases—enterostomy against nonenterostomy.

TABLE 5—*Percentage of Enterostomy Cases in Each Time Group, From Presbyterian Hospital Statistics, 1916-1923, Inclusive*

Time Group, Hours	Total Cases in Time Group	Nonenterostomies†	Enterostomies	Percentage of Enterostomies in Each Group
12	2	1	1	50
12 to 24	16	7	9	56
24 to 48	20	14	6	30
48 to 72	23	12	11	48
72+	79	48	31	40
Totals	140	82	58*	

* Out of fifty eight enterostomies only sixteen were performed within forty-eight hours after onset and thirty one (more than half) were done on late cases.

† The nonenterostomy group has 73 per cent of cases after forty eight hours. The enterostomy group has 72.4 per cent of cases after forty-eight hours.

TABLE 6—*Comparison Between Mortality of Entire Enterostomy Group and Entire Nonenterostomy Group, Taken from the Presbyterian Hospital Statistics*

Of the series of one hundred and forty acute ileus cases (1916-1923, inc.) fifty eight patients had enterostomies and eighty two did not.

	Total Cases	Recovered	Died	Mortality
Entire enterostomy group	58	12	46	79.2%
Entire nonenterostomy group	82	44	38	46.3%

TABLE 7—*Comparative Mortality of Enterostomy Late Group and Nonenterostomy Late Group, Taken from the Presbyterian Hospital Statistics*

The time group operated on more than forty-eight hours after onset comprised fifty three cases (in the years 1923-1923, inc.). Of these, thirty patients had enterostomies and twenty three did not.

	Total Cases	Recovered	Died	Mortality
Enterostomy group	30	12	18	60%
Nonenterostomy group	23	12	11	47.8%

Again, we find the former decidedly higher. This tends to confirm the previous observations. If enterostomy is as valuable as it is said to be, one would expect to find the mortality rate of the group so treated (other factors being equal) lower than that of the nonenterostomy group. However the other factors have probably not been equal, and enterostomy has generally been performed with or in sequence to an exploratory or relief operation as well as on the sickest patients or on those with acute ileus in an advanced stage. The poor choice of cases and the additional shock of the added procedure may account largely for the higher

mortality rate. Certainly enterostomy has not infrequently been performed as a last resort on patients who were in a critical condition following a relief operation, and who would probably have died anyway. The mortality rate could have been credited to the nonenterostomy group had not the enterostomy been performed in the unjustified hope of saving the patient. Enterostomy has been similarly performed on almost moribund patients who were thought not be able to tolerate further severe surgical procedures. Since enterostomy has frequently been performed without proper appreciation of its limitations, an undeserved appearance of danger has been given to the procedure.

Enterostomy is not a "sure cure," nor is there any magic about it. Like other surgical procedures, it must be performed in the right way and at the right time to be effective. In cases in which the patient has acute ileus in an advanced stage, the condition is primarily chemical, and purely mechanical treatment cannot be effective. The ileus poison has presumably been absorbed into the blood and tissues. It would be as unreasonable to expect the condition of the patient to improve after enterostomy had been performed in these cases as to expect a person to recover who had already absorbed a lethal dose of any other poison. It is also unreasonable to add surgical shock to fatal chemical poisoning. The primary object of enterostomy in the treatment of acute ileus is to secure drainage. Even if enterostomy is performed in time but a drainage is not obtained, the procedure is without value. If drainage is not secured at the end of twenty-four hours, the enterostomy should be carefully investigated and if necessary revised, however, this is rarely done, and in cases in which the condition is far advanced there is often little time for it. We feel that the considerations cited tend to explain why the statistical evidence we have collected does not serve to support the general enthusiasm for enterostomy. It is interesting to find this discrepancy between the statistical evidence and the general belief in the efficacy of enterostomy, it is of some importance to record it, but of far greater importance to call attention to the fact that statistics such as those we have collected can never be used to demonstrate the efficacy of enterostomy (if it is actually efficacious) in lowering the mortality rate in acute ileus. The reason for this is that the time factor, which is of primary importance in the mortality rate of patients with acute ileus, has not been recorded, and cannot be taken into consideration.

GROUP COMPARISON

Improvement can be shown only by fair comparison of one surgical group with another. A fair comparison of the results to determine the influence of one procedure or another on them cannot be made without taking the time factor into consideration, and the time factor has not

taken into consideration unless the statistics are so analyzed as to make this possible. For example, in comparing two series, the following points should be noted: (a) the number of cases in the enterostomy group and in the nonenterostomy group of each series, that is, each series should be divided into an enterostomy and a nonenterostomy group, (b) the percentage of early cases (operated on within forty-eight hours after onset) in each entire series, (c) the percentage of early cases in each enterostomy group, (d) the percentage of early cases in each nonenterostomy group, (e) the mortality percentage of each entire series, (f) the mortality percentage of each enterostomy group, (g) the mortality percentage of each nonenterostomy group. These determinations are required to check the time factor (early operation) and the technic factor (enterostomy or nonenterostomy) as they affect the results of the operation expressed in terms of the mortality rate. Only after having secured them is one in a position to make a fair comparison of the technical results or to estimate whether any degree of improvement may be due to enterostomy. A lower mortality rate in one series cannot be said to indicate better technical results unless it is shown that this series has the same percentage (approximately) of late cases as that with which it is compared. Neither can it be said that lower mortality rate in one series is due to the effects of enterostomy unless it is shown that the improvement was not due to the time factor nor to better technic in the nonenterostomy group. It cannot be asserted that lower mortality rates in one enterostomy group is due to better technic until the time factor has been discounted by a percentage comparison of the early cases in the two groups being compared.

On the other hand, if one can show that two series each comprised the same percentage of late cases, it is fair to say that the lower mortality rate of one is probably due to better technic. Again, if one can show that the time factor was the same in two series, as well as in their respective enterostomy and nonenterostomy groups, and if one can show also that there was no material improvement in the nonenterostomy group the lower mortality of one series can properly be attributed to the beneficial effect of enterostomy.

To summarize. Each series of cases of acute ileus is divided into two groups—an enterostomy and a nonenterostomy group. If the mortality rate of the entire series is lowered (and that of the enterostomy group as well) the mortality rate of the nonenterostomy group must remain relatively unchanged (or be higher than before), else the improvement in the rate cannot be ascribed definitely to the enterostomy group. The two enterostomy groups should be analyzed (being compared) as to whether the patient has ileus in an early or advanced stage. If the group with the lower mortality rate contains a larger proportion of early cases

than does the other, the improvement must be ascribed rather to earlier treatment than to improved technic. Granted that early treatment brings better results, in comparing the general mortality of any two entire series they must be analyzed for early and late cases. If the one with lower mortality rate comprises a greater proportion of early cases than the other, the improvement is ascribed again to early diagnosis rather than to any special procedure such as enterostomy. Therefore, in order to prove the efficacy of enterostomy in lowering the mortality rate in cases of acute ileus, the mortality rate of the series for all cases must be lowered in addition to the lowering of the mortality of the enterostomy group in that same series, while the mortality of the nonenterostomy group remains relatively unchanged, and the entire series as well as its enterostomy group shows approximately the same percentage of early and late cases as those with which they are compared. When the statistics for acute ileus compiled by Gibson in 1900 are compared with those compiled

TABLE 8—*Comparison of Mortality by Four-Year Periods in the Same Hospital*

Taken from the Presbyterian Hospital statistics. Note that the largest percentage of improvement is found in the nonenterostomy group.

Cases Referred to	Number of Cases		Mortality Percentage	
	1916-1919	1920-1923	1916-1919	1920-1923
Entire series	60	80	66.6	73.7
Nonenterostomy group	38	44	52.6	31.0
Enterostomy group	22	36	90.9	77.7

by us in 1925 (table 3), the mortality rate of the recent enterostomy group is found to be 3.5 per cent lower than that of twenty-seven years ago, and the mortality rate of the entire recent series is 1.4 per cent lower than that of twenty-seven years ago, but the mortality rate of the nonenterostomy group is 5.2 per cent better than in the old series. Here then the mortality rate of the entire series has apparently been lowered chiefly by lowering that in the nonenterostomy group. Any reduction in mortality ascribable to enterostomy has probably been apparent rather than real, and is probably due to the selection of earlier cases. This is a deduction, not a demonstration, because we lack evidence as to the time factor. Our own series at the Presbyterian Hospital shows similar indications (table 8). In the entire four year series the mortality rate has been lowered 12.9 per cent while the mortality rate of the enterostomy group has been lowered 13.2 per cent. At the same time however the mortality rate of nonenterostomy cases has been lowered 18.6 per cent. It is evident that the improved mortality rate of the nonenterostomy group is chiefly responsible for the improved mortality rate of the entire four year series which therefore can be due only in small part to a lowered mortality rate of the enterostomy group.

In analyzing the two four year series reported from the Presbyterian Hospital for early and late cases (table 9, dagger footnote), we find that the first series included 15 per cent more late cases than the second series. We ascribe the improvement in the mortality rate of the second series to early treatment rather than to improved operative technic or to any special procedure such as enterostomy. Moreover, the improvement in the mortality rate of the enterostomy group cannot be justifiably ascribed

TABLE 9—*Rise in Mortality Due to Late Operation Group Mortality in Hours After Onset, Comparison by Four-Year Periods*

Taken from the Presbyterian Hospital statistics Time analysis of the two four-year series shown in table 8

Percentage Mortality	Hours Between Onset and Operation				
	12	24	48	72	72+
90	1				
80					38
70				12	
60			15		
50				11	41
40		11			
30		5	5		
20					
10					
	1				

Light faced figures represent series of 1916-1919, inclusive, mortality, 66.6 per cent (1916-1919 series includes about 15 per cent more late cases [after forty-eight hours] than does 1920-1923 series). Bold faced figures represent series of 1920-1923, inclusive, mortality, 53.7 per cent. The numbers show the number of cases in which operation was performed in the twelve or twenty-four hour period.

* Compare these curves with that in table 4

TABLE 10—*Analysis of Enterostomy Groups by Hours After Onset*

Taken from the Presbyterian Hospital four year series shown in tables 6 and 7

Years 1916-1919 Inclusive	Years 1920-1923 Inclusive
1 12 hour case	0 12 hours cases
4 12 to 24 hour cases	5 12 to 24 hour cases
3 24 to 48 hour cases	3 24 to 48 hour cases
2 48 to 72 hour cases	9 48 to 72 hour cases
12 72+ cases	21 72+ cases
22 cases, mortality 90.9%	38 cases, mortality 77.7%
63.5% of cases were over 48 hours	78.9% of cases were over 48 hours

to the enterostomy procedure until we have decided whether the lower mortality is due to better technic or to earlier operation. In analyzing the two enterostomy groups for early and late cases (table 10), we find that the second group has a larger percentage of late cases than the first group. It should therefore (other things being equal) have a higher mortality rate, we find that it has a lower mortality than the first group. We may then, justly ascribe the improvement to better technic rather than to earlier operation. Here is statistical evidence indicating that enterostomy has saved some patients with acute ileus who might have

died. It is good evidence, because it was obtained after satisfying the criteria on which a just comparison depends.

SUMMARY

Enterostomy as a treatment for acute ileus has been used in only a small percentage of the total number of cases. It has apparently been reserved as a last resort in the cases in which the patient is the sickest and the condition is most advanced. There is evidence suggesting that this procedure has been effective in lowering the mortality rate, but it has apparently had little influence on the general mortality rate of all cases in a series. If it is to affect this rate (supposing it to be capable of so doing) it must be used in a larger percentage of the total number of cases in a series—in the early as well as in the late groups and more often as a preliminary step to further treatment.

The actual value of enterostomy as a treatment for acute ileus must be determined ultimately by statistical proof. Statistics published up to this time do not afford a satisfactory basis for comparison except in a few instances, those are too few for definite conclusions.

Because of the recognized effect that early opposition has on the mortality of the condition, any series of cases of acute ileus (in order fairly to compare its results with those of another series) must be analyzed into its component groups of early and late cases. This is true also of the enterostomy and nonenterostomy groups in the series of cases of acute ileus. It is hoped that those who are interested in acute ileus will record and publish their series of cases in such a manner that comparisons can satisfactorily be made with a view to establishing definitely the value of enterostomy in the treatment of this condition. The desirability of doing this has been indicated in a recent publication on experimental work by Haden and Orr¹⁸

¹⁸ Haden and Orr. High Jejunostomy in Intestinal Obstruction, *J. A. M. A.* 87:632 (Aug. 28) 1926.

A REVIEW OF UROLOGIC SURGERY

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(Concluded from page 154)

PROSTATE

Prostatectomy—Tengwall⁴² performs prostatectomy according to Freyer's technic. The retention catheter is used for bladder drainage. In his first 150 cases no packs were used. One patient died from hemorrhage, and seven had severe postoperative hemorrhage which necessitated reopening the bladder. In the last 100 cases, packs were placed in the prostatic bed, and there was no hemorrhage. The packs were removed in forty-eight hours, and the bladder drained in three or four days. A urethral retention catheter was left in place until the operative wound healed, so that there would be no strain on the wound. In the first fifty cases Tengwall used spinal anesthesia with 3 per cent tiopocain. One patient died from shock. In 140 cases local anesthesia was used to open the bladder, after which the prostatic bed of the bladder was infiltrated with procaine hydrochloride, according to Legueu. In 140 cases in which operation was performed prior to 1918, tests of renal function were not performed, five deaths occurred from uremia. In the last 110 cases in which various tests of renal function were made, there were but two deaths from uremia. Pre-operative preparation and forced fluids were emphasized. In all cases examination was made with the stone probe and if vesical neoplasm was considered, cystoscopy was carried out. If the results of tests by water dilution were good there being no further contraindication, the patient

⁴² Tengwall Ernest. Two Hundred Fifty Suprapubic Prostatectomies for Hypertrophy of the Prostate. *Acta chir Scandinav* 59 455, 1926, *Hygier* 87 795 1925, abstr. *Ztschr f urol Chir* 20 173, 1926.

was operated on at once. If results of the water test were poor, drainage was instituted until the renal function improved. If there was no improvement in from four to six weeks, a suprapubic drainage was made, and prostatectomy performed later (in twenty-three cases there was one death). Old age was not a contraindication to operation. Twenty-five patients were more than 80 years old.

In 145 cases only one case of cancer was revealed on histologic examination. In more than half the cases, the urine was badly infected. As the best combatant to this infection Tengwall advised bladder lavage with from 0.5 to 2 per cent silver nitrate solution. In fifty-one of seventy-nine cases the urine prior to operation was infected. Postoperatively, the urine was infected in twenty-seven and normal in fifty-two. Twenty-seven (10.8 per cent) of the patients died. One hundred eighty-eight patients were traced, of whom 180 had improved, two were slightly better, and six were worse.

In seven cases death was due to uremia, in two to hemorrhage, in one to shock following spinal anesthesia, in five to sepsis, in three to pyelonephritis, in four to bronchopneumonia, in three to pulmonary embolism, in one to cerebral embolus and in one to heart failure. The residual urine was tested in 112 cases. In seventy cases there was none, in thirty-six there was from 5 to 50 cc., in three, 75 cc., in two 100 cc., and in one 150 cc. Postoperative stricture developed in seven cases. In fifty-four (23 per cent) epididymitis developed, in nine of which suppuration occurred, in four cases hernias developed in the wound. Sexual function was noted in seventy-four cases. Thirty patients were impotent before operation, twenty-eight were normal after operation, two lost function after operation, four patients had normal function, but no ejaculation. One 65 year old man impregnated his wife after operation.

Cohen, Dodds, and Webb⁴ assert that the nonprotein nitrogen and uric acid content of the blood are the most accurate guides to prognosis. The upper limit of safety for complete operation of prostatectomy was found to be 50 mg. for each hundred cubic centimeters of nonprotein nitrogen, and 3.5 mg. for each hundred cubic centimeters for uric acid. Experience has shown that if figures above these are encountered it is advisable to perform preliminary suprapubic cystotomy. Enucleation can then be carried out when the figures fall within the limits of safety. The urea content in the blood is much more unreliable than the nonprotein nitrogen and uric acid contents. A high urea content in the blood must always be regarded as a serious sign, but reference to the tables will show that a low urea content cannot always be

43. Cohen I., Dodds F. C. and Webb C. H. S.: Observations on the Results of the Operation of Prostatectomy. *Brit. J. Surg.* **13**: 655, 1926.

regarded as an indication of normal renal function. Laboratory data alone should never be relied on, but should always be considered in combination with the clinical state of the patient.

Punch Operation—Van Houtum⁴⁴ summarized the treatment of median bar and vesical neck contracture, mentioning especially Caulk's cautery punch. He treated thirteen patients with Caulk's punch, eleven obtained good results, one remained unchanged, and one died, supposedly from ether anesthesia. Parasacral anesthesia was used in the other cases.

Van Houtum believes that from one fourth to one third of all cases of prostatitis are suited to the punch operation. There are of course many borderline cases in which there is a question of using a punch or performing a prostatectomy. The type of procedure is influenced by the social status of the patient, the experience of the surgeon and the general symptoms. It should be remembered that a prostate may often recede after the urinary stream has been reestablished, and if the punch is not successful prostatectomy can always be performed.

Complications—Randall⁴⁵ points out the failure to realize the extreme importance of some of the so-called lesser postoperative complications. He bases his conclusions on the investigation of a series of 100 cases of prostatectomy in relation to the occurrence of epididymitis. White is quoted as reporting the occurrence of this complication in 82 per cent of fifty cases which he investigated. Eisendrath found the complication in one-fifth of his cases. In Randall's experience it occurred in twenty-three cases in the 500. In four cases it was associated with perineal prostatectomy, and in nineteen the suprapubic operation had been performed. The time of occurrence of the epididymitis varied from five cases preoperatively to six cases after the patient had returned home. As a rule, it occurred just as urethral voiding was reestablished.

Epididymitis was about as common in private patients as in ward patients. There were three deaths in the series, in each case, however, there was some other complication. Healing was generally delayed in cases in which epididymitis developed.

Randall advises support and hot magnesium sulphate compresses, followed later by the application of 5 per cent guaiacol ointment. He believes that careful daily irrigations would do a good deal toward preventing the occurrence of this complication and he also advises further study of the effects of ligating the vas.

44 Van Houtum G. Erfahrungen mit der Caulkschen Punch-Operation bei kleinen Prostaten, *Ztschr f urol Chir* 19 253, 1926.

45 Randall Alexander. The Role of Epididymitis as a Complication of Prostatectomy, *J Urol* 16 141, 1926.

Prostatic Sarcoma—Smith and Torgerson⁴⁶ reviewed the literature on sarcoma of the prostate and reported eighty-four cases, including one case of their own. Sarcoma of the prostate occurs in adult life in about 65 per cent of cases, in 30 per cent the disease occurs in the first ten years of life. The first symptoms are usually related either to the rectum or the bladder, and are in the form of partial obstruction of the bowel, difficulty in urination or complete retention. Pain, which sooner or later almost always appears, is of two types, that produced by obstruction of the rectum or bladder, and essential pain, severe lancinating and interfering with rest and sleep, deep in the pelvis and not dependent on urination or defecation. The pain may radiate in almost any direction, but its common course is through the sacrum or down the limbs to the knees. Hematuria is sometimes present and is due either to ulceration of the bladder or diffusion of the growth throughout the wall. The tumor varies markedly in size. As a rule on rectal examination, the prostate is found greatly enlarged, particularly in the child. It is usually smooth and firm, although it is sometimes cystic or soft.

The round cell type is the most common, the spindle type is next. Metastasis was noted in about 40 per cent of cases. Distant metastasis is quite rare in early life. Local extension occurred in fifty-nine cases (72 per cent). The bladder was most often involved, extension to this structure occurring in forty-one (70 per cent) of the cases. In twenty-three cases (40 per cent) the urethra was involved, and in eleven cases the rectum. Treatment is not satisfactory and the outlook is poor. All the patients in this series died from the disease.

BLADDER

Tumors—Simon⁴⁷ reports seventy-three operations for carcinoma of the bladder performed on fifty patients. Twenty-four of the patients (48 per cent) are alive and twenty-six (52 per cent) are dead. In twelve of the latter a radical operation could not be performed. Twenty-two of the twenty-four living patients had papillomatous tumors, only two tumors were of the infiltrating type. Eight of the twenty-six patients who died had infiltrating tumors.

According to Judd⁴⁸ the results of radical operation for carcinoma of the bladder have not come up to expectations, they are about the same as those obtained in radical operations for carcinoma of the breast, stomach

46 Smith, R. R. and Torgerson, W. R. Sarcoma of the Prostate. Report of a Case with a Digest of the Literature. *Surg. Gynec. and Obst.* **43**: 225, 1922.

47 Simon, L. Die Behandlung und Prognose der malignen Blasen-Tumoren. *Beitr. z. klin. Chir.* **136**: 565, 1926.

48 Judd, E. S. The Treatment of Carcinoma of the Bladder. *Ann. Surg.* **41**: 5, 1925. *Surgical Methods*. J. A. M. A. **87**: 1620 (Nov. 13), 1926.

colon and other organs. Seven hundred and eight cases of carcinoma of the bladder from the Mayo Clinic are reviewed. Two hundred and thirty-eight of the patients are known to be living. Ninety-four have lived three years or more, sixty-two, five years or more, and five, ten years. Fifty of 298 patients who had surgical treatment alone or surgical treatment with radium lived more than five years, and twenty-eight of 308 patients who had other forms of treatment lived more than five years.

In 261 of the 272 patients traced, the tumors were graded according to the degree of malignancy. Of twenty-one patients with tumors graded 1, sixteen are living, three have died since leaving the hospital, of eighty-one with tumors graded 2, thirty-eight are living, thirty have died since leaving the hospital, of 103 with tumors graded 3, twenty-seven are living, sixty-two have died since leaving the hospital, of fifty-six with tumors graded 4, sixteen are living, thirty-two are known to have died after they reached home. Five patients lived ten years, in one malignancy was graded 3, in two it was graded 4, and in two, 1.

Of the 708 cases, 102 were too far advanced, or the patient was in too poor general condition to warrant any kind of treatment. The average duration of the disease in the 102 cases was thirty-two months and the average length of life after the examination was eight and nine-tenths months at the time of publication of the report. Forty-three of the 708 patients were treated by radium and fulguration, and this group showed the highest average length of life after treatment, which was thirty-six and seven-tenths months. Fourteen were treated with radium and cautery, and the average duration of life afterward was ten and seven-tenths months, which was but little longer than in those who were not treated. But this figure is deceiving, for some of the best results have been obtained by the use of the cautery in cases in which the disease seemed well advanced. Seventy-nine patients were treated with radium combined with excision or resection, and they lived, on an average, twenty-one and fifty-six hundredths months afterward. Of the 708 patients, 219 received surgical treatment alone, and the average postoperative length of life was eighteen and fifty-seven hundredths months, nineteen of the 708 were treated by surgical diathermy. The time since treatment is too short to determine what the ultimate results will be. However, the immediate results in some of the cases in which the disease was extensive have been extremely gratifying.

From the standpoint of treatment, Judd divides tumors of the bladder into three groups. The first group should include cases of benign tumor. Most of such tumors are papillomas and should be treated by endoscopic methods. The second group should include all malignant cases in which the process is still confined to the bladder and all cases in which the diagnosis is questionable. The treatment indicated is

radical removal of the growth and reconstruction of the bladder if that is possible. In the third group should be placed cases in which the malignant growth is too extensive for removal. If the lesion is confined to the bladder it can be removed by radical operation, but if it has extended to the perivesical tissues, fixing the bladder firmly to the prostate and seminal vesicles or to the other organs in the pelvis it is not advisable to attempt to remove it. For growths too extensive for radical removal, surgical diathermy is the best procedure. Such treatment should be carried out in cases in which the carcinoma of the bladder is less extensive, if there is some contraindication to the radical operation, such as cardiac or renal disease.

Ureteral Transplantation—Chute⁴⁹ believes that more radical measures must be adopted, such as transplantation of the ureters, if better results are to be secured in cases of carcinoma of the bladder. In eighty-six of 170 of Chute's operative cases the patients are known to have died as a result of operation or disease; eighteen others had recurrences. Another fact is taken into account in considering the results in Chute's cases, that a large percentage of the patients, nearly one-third, on whom an open operation was performed and who are not known to have died, had been treated for so-called simple papillomas, often quite small, a number of years previously. Such cases are at present not subjected to open operation, but are more satisfactorily treated by fulguration.

Chute reports five cases of cystectomy for carcinoma, all the patients died. In one case a large pocket of pus was found deep in the pelvis near the right ureter. In the second case death was due to pyelonephritis and sepsis from a sloughing pelvic cavity. There was necrosis of the sigmoid at the site of ureteral transplant in the third case. Death resulted from embolic pneumonia in the fourth case. Necropsy was not obtained in the last case.

In spite of the poor results obtained in his cases Chute firmly believes that total cystectomy, either preceded or followed by transplantation of the ureters, is the best way of dealing with extensive infiltrating tumors of the bladder, stubborn recurring growths of the papillomatous type and growths which involve the outlet of the bladder. He says that prostatecystectomy is probably the operation of choice for men. He discusses the Coffey technic of implantation of the ureters into the rectum.

Hinman⁵⁰ believes in transplanting the ureters into the bladder in a small group of cases. Although the method is now usually employed

49 Chute, A. L. Ureteral Transplantation in Bladder Cancer. *Ann. Surg.* **87** 1613 (Nov. 13) 1926.

50 Hinman, Frank. The Indication of Nephrectomy in Bladder Cancer. *Ann. Surg.* **86** 921 (March 27) 1927.

only as a last resort, if freed from some of its immediate and remote dangers it could be applied to a larger number of cases. The procedure is most common in cases of exstrophy of the bladder, but even in this type of case it is not entirely satisfactory, as after the transplantation further urologic study of the part is not possible, in one case after transplantation a stone blocked the ureter and could not be reached through the rectum. Hinman believes that a surgical victory over this defect must include a restoration of natural relationships, that is, repairing the cleft symphysis as one would repair a cleft palate.

Ureteral transplantation is indicated in certain acquired conditions, such as extensive vesical carcinoma, necessitating total cystectomy. Transplantation should also be performed in cases of extensive tuberculosis of the bladder, if an infected kidney has been removed and the patient is suffering from frequency and pain. Unless this is done the bladder contracts the ureteral orifice, causing dilatation of the remaining kidney. In several cases, hydronephrosis was found in the remaining kidney without any sign of tuberculosis.

Carcinoma of the uterus may necessitate radical resection, and sometimes the ureters are involved. Usually the surgeon ties the ureter and then removes the kidney. If uretero-intestinal anastomosis were a safe procedure more radical measures might be undertaken. The rectum is a better site for the transplant than the skin, since it gives continence. The difficulties of a successful transplant of the ureter are inherent and technical, and immediate and remote. The inherent objections are putting the ureters in an infected field in which urologic studies cannot be carried out. The technical ones, such as the spread of infection, peritonitis and fecal fistula, may be overcome. The immediate dangers result from the edema at the site of the transplant which causes ureteral obstruction and ascending pyelonephritis or anuria.

To insure satisfactory renal function Hinman advocates a first-stage, preparatory nephrostomy, followed subsequently by ureteral transplantation. Lumbar drainage permits direct treatment and free drainage of the kidney. At the same time the ureter could be treated after the transplantation by irrigation and dilatation. Hinman has used this procedure with success in two cases.

Injuries to the Bladder—Peacock and Ham⁵¹ discuss the problems associated with injuries of the urethra and bladder. Straddle falls although a common cause of such injuries, are not so common as in the past. The advent of certain industrial hazards and the automobile have given crushing injuries a larger place in the etiology of these conditions. Industrial accidents account for 55 per cent of the cases reported

⁵¹ Peacock A. H. and Ham R. F. Injuries of the Urethra and Bladder. A Study of Thirteen Cases. *J. Urol.* **15**: 563, 1926.

by these authors. Automobile accidents were etiologic factors in 18.7 per cent of the industrial and 50 per cent of the nonindustrial accidents. Crushing injuries accounted for 46.4 per cent of the cases and straddle injuries only 17.4 per cent. Fracture of the pelvis was common associated with injury of the urethra, although the urethra was uninjured in a majority of fractures of the pelvis. Gunshot wounds are rare in civil life. Automutilation is seldom seen except among insane patients.

It is not surprising that 89 per cent of the injuries of the bladder and urethra occurred in men, possibly because of their greater activity, their occupational hazards and the close anatomic relation of the urethra to the pubic arch. The urethra is firmly fixed to this bridge of bone, and any fracture or displacement of the latter is likely to tear across the urethra. In women the urethra is shorter, less firmly attached and moves with the anterior vaginal wall.

Latent symptoms in order of occurrence are dysuria, frequency of urination, loss in strength, urinary infection, impairment of sexual power, hematuria, periodical retention and backache.

Immediate operation, such as suprapubic cystotomy, retention catheter, suprapubic cystotomy and laparotomy, and suprapubic puncture, may be required, while late operations are dilatation with sounds or bougies, combined suprapubic cystotomy and external urethrotomy.

The average time in the hospital is sixteen weeks. The average period of disability is twenty-three months.

The automobile is directly responsible for one-third of these injuries. The industrial disability phase is important as it involves extensive hospitalization, loss of time, and only 33 per cent of the patients can be called cured. Fifty-five per cent of the patients were entitled to industrial compensation.

Ectrophy—Mayo and Hendricks⁵² report sixty-six cases of ectrophy of the bladder in which operation was performed at the Mayo Clinic between 1901 and 1926. Forty-eight of the patients are living and eighteen are dead. Plastic operation alone for closure of the bladder was performed in eight cases; transplantation of both ureters in four cases; transplantation of one ureter in nine cases; exploration and closure because of hydro-ureter or hydronephrosis in two cases; transplantation of one ureter to the hepatic flexure in one case; suprapubic cystostomy for excision of carcinoma of the bladder in one case; the Mowman operation in two cases; and the recent Coffey operation in three cases. In two of these both ureters were transplanted simultaneously and in the other one ureter was transplanted. Of the patients 16.6 per cent died in the hospital, eleven recovered.

⁵² Mayo, C. H. and Hendricks, W. A. *Ectrophy of the bladder*. *Ann. Surg.* 1927, 85: 555.
Gynec. Obst. 43: 129, 1926.

nineteen days after operation. Five patients died from peritonitis, and six died from urinary infection, hydro-uretero-nephrosis and uremia. Complete statistics were obtained concerning twenty-nine patients. Twenty-nine were satisfied with the results. Two had poor control of urine by rectum. The period between emptying the rectum varied from two to five hours by day and from three to eight by night. One patient was incontinent. Bowel movements varied from five to six times a day to once or twice. The general health of the patients was invariably good, most of them had gained in weight, had good appetites and slept well. Six of the twenty-nine patients are living from one to three years after operation, ten are living from three to six years, ten are living from six to twelve years, and three are living from twelve to fifteen years.

Vesico-ovarian Fistula—Fronstein and Sserdjukoff⁵³ describe a case of vesico-ovarian fistula in a woman, aged 38. The rupture of purulent abscesses in the parametrium, of suppurating dermoid cysts, of ectopic pregnancy and of suppurating tubal abscesses, into the bladder is not infrequently described, but according to these authors there is no literature on vesico-ovarian fistula, and in this respect their case is unique.

The clinical picture of the rupture of any pelvic abscess into the bladder begins with frequency and dysuria, due to inflammatory infiltration of the wall of the bladder. At this stage cystoscopy reveals bullous edema of the wall at the affected site. With the concurrence of rupture, the urine becomes loaded with pus. There is improvement in the subjective symptoms, the temperature falls, and the cystoscope shows a point of rupture usually of small diameter, surrounded by edematous mucosa. Frequently pus may be found trickling from the point of rupture. The course of the disease then becomes intermittent. If there is good drainage of the pus into the bladder, the subjective symptoms and the temperature are more favorable, and there is little pain. With occlusion of the point of rupture, from time to time, the urine becomes clear but there is pain and fever with dysuria. Frequently and early in the course of the disease, an ascending infection of the kidneys develops.

Conservative treatment includes lavage of the bladder, drainage of the pelvic abscess by vaginal or abdominal routes or the attempt to clear up the inflammatory mass by nonspecific protein therapy. With the subsidence of the pelvic infection under such treatment the vesical fistula frequently heals, but this end-result is by no means certain. Radical excision of the perforating mass together with the vesical fistula, and the suture of the bladder although attended by greater operative risk, are necessary when conservative methods fail.

⁵³ Fronstein R, and Sserdjukoff M. Zur Frage der Ovarial-Blasenfisteln. *Ztschr f urol Chir* 19 102 1926.

In the authors' case a large ovarian abscess on the right side had ruptured into the bladder by way of the right broad ligament. Bilateral salpingitis, suppurative oophoritis and myometritis were present. After one and a half months of conservative treatment including repeated intravenous injections of methenamine solution, the fistula persisted and symptoms were only slightly improved. Laparotomy was performed with resection of the adnexa, of the abscess and of the fistulous tract which was found to be connected with the ovary. The bladder was sutured, the abdomen closed and an indwelling urethral catheter inserted for six days. The convalescence was marked by a probable intarct of the stomach, clinically suggested by nausea, coffee-ground vomitus and pain in the region of the greater curvature. This cleared up shortly, and the patient recovered satisfactorily. On examination after five months there was no marked inflammatory process in the bladder or vagina.

[ED. NOTE—The vesico-ovarian fistula described here is unusual although it is remarkable that more cases have not been noted. The danger of radical operation by laparotomy is obviously that of spreading the infection into the general peritoneum. Franks and Sordjnikoff used ether to wash out the pelvis at the completion of the operation before closure. When dealing with large pelvic masses which cannot be properly drained through the vagina, and when conservative methods do not result in prompt improvement, probably the best recourse will be that of radical resection as described.]

Infections of the Bladder—Dickson⁷⁴ reports the case of a woman aged 37, who had suffered from a urinary infection for many years. In 1916, sporelike bodies together with other organisms were found both in the urine from the bladder and in that from the ureter. Corresponding with this fungus-like organism a pleomorphic organism was sometimes found in the cultures, but it was grown with extreme difficulty and soon died out in the cultures. Similar observations were made from time to time, and on May 6, 1925, a small shred or clump of large irregular cells, containing numerous vacuoles, was found. When these were examined wet and faintly stained with methylene blue and other stains they contained apparently structureless, clear rounded or slightly oval bodies or inclusions which strongly suggested the so-called Malakoplakia Gutmann bodies or malakoplakia.

Fresh wet preparations of the centrifugized deposit of the sediment showed considerable numbers of large cells containing the cells already mentioned. These inclusions varied greatly in size from a few microns or even more. When still fresh they appeared as

74. Dickson W. F. C. Demonstration of a New Type of Infection in the Bladder in a Case Resembling Malakoplakia. *Proc. Roy. Soc. Med.* 18: 1925.

structureless, homogeneous; rounded or slightly oval, and occasionally sausage-shaped, retractile and slightly greenish, and with a definite-clear-cut outline. In a few hours little mycelial filaments began to sprout, and soon every cell appeared like germinating peas, the thickness of the filaments varying from 1 to 5 microns, or even more. The growth was so rapid that a slow, snakelike writhing movement was seen distinctly on two occasions. Yeastlike budding was also present. As the original cells of the exudate gradually disintegrated, numerous spherical bodies were set free and passed into the fluid, these varied in size up to 12 microns, or even more, in diameter.

Patches resembling malakoplakia were seen in the bladder through the cystoscope, and specimens were snipped out for examination. Wet preparations of these exhibited the same curious organism in many of its forms. The most numerous were the perfectly spherical, hyaline, structureless bodies which can best be described as resembling little drops of oil.

Blanc⁵⁵ states that in the treatment of vesical tuberculosis with methylene blue the dye must be chemically pure, entirely dissolved and filtered before using. Satisfactory solutions make a homogeneous blue stain on linen, while inferior solutions give a pale blue tint which may be surrounded with unstained areas. A 1:100 solution is made in normal sodium chloride solution and must be tepid on instillation. One may begin with from 5 to 10 cc., but if bladders are intolerant the amount may be reduced or a weaker solution may be used at the start, after which the concentration and amount may be increased gradually. In the presence of strong pyuria, the bladder should be irrigated with a 1:4,000 to 1:8,000 oxycyanide of mercury solution before instillation. A Nelaton catheter is used for women, and a small Guyon catheter for men. After such an instillation the patient should move about, since by so doing he may be better able to retain the instillation.

Herpes of the Bladder.—According to Schiffmann,⁵⁶ there has been much confusion in the literature as to just what has been designated herpes of the bladder. Lipschutz has shown by experiments in vaccination that herpes genitalis is an infectious process of the skin and mucous membrane. It is closely related to herpes febrilis and herpes zoster, but must be differentiated from them.

Schiffmann reports the case of a woman, aged 31, who had a general eruption about the genitals, which proved to be a typical herpes. The vagina and mucous membranes were normal. Later the genitals were completely covered and edematous. Complete retention developed, and

⁵⁵ Blanc, Henry. La technique des instillations vesicales de bleu de méthylène dans la cystite tuberculeuse, *J. d'urologie* **20** 144, 1925.

⁵⁶ Schiffmann, Josef. Herpes der Blase, *Ztschr. f. urol. Chir.* **19** 342, 1926.

catheterization was necessary. The urine contained red blood cells and small clumps of pus. Culture of the urine was sterile. This condition persisted for four weeks and a half, during which time the bladder was washed. There was no cystoscopic examination; nevertheless, Schiffmann believes that the case is herpes of the bladder because of the outer manifestations and a definite resistance encountered at the vesical neck, which was attributed to blebs. The retention was reflex, probably because of the pain from the herpes genitalis. As the latter healed, normal miction was reestablished.

Du Bois⁵⁷ submits a case of "herpes zoster of the bladder," the diagnosis being based on the cystoscopic data of typical herpetic vesicles coincident with a typical herpes zoster of the buttock, of the same side. It is noteworthy that the nerve supply of the buttock and of the base of the bladder is the same, that is, from the sacral plexus. He believes that the diagnosis is further confirmed by the more or less rapid disappearance of both the cutaneous and mucosal lesions at the same time, without any particular treatment, other than by mild urinary antiseptics and a local application of methylene blue to the external lesions.

Nishimura⁵⁸ states that varices of the bladder are not common. Prior to the advent of the cystoscope, diagnosis could be made only at necropsy. The condition has been designated "bladder hemorrhoids." For the most part it is only an expression of venous stasis in the pelvic organs. Certain observers have noted that bleeding seldom occurs, but sometimes with disturbed menstruation the varices may cause vicarious bleeding from the bladder. A case is cited in which there was hematuria, and cystoscopy revealed varicose veins of the bladder and a coagulum at the base. Since the patient had hemorrhoids, it was assumed that the two were associated. In treating these patients the retention catheter, ergotin, chlorcalcium intravenously or by mouth, or the high frequency current may be used. Should these be inadequate, suprapubic cystotomy is indicated.

URETHRA

Tuberculosis—Richter⁵⁹ reports the following cases. A man, aged 47, had had symptoms of renal tuberculosis for one and a half years, and recently tuberculous epididymitis had developed. There were no subjective symptoms of urethral stricture, but following the passage of several sounds acute military tuberculosis appeared, and the patient died.

57. Du Bois, F. E. A Case of Herpes Zoster of the Bladder. *J. Urol.* **15**: 557, 1926.

58. Nishimura, Kōichi. Les varices vésicales. *Act. Derm.* **6**: 225, 1925. *Ztschr. f. urol. Chir.* **19**: 359, 1926.

59. Richter, Solver. Zur Kenntnis der Herpes genitalis. *Acta chir. Scand.* **59**: 277, 1925. *Ztschr. f. urol. Chir.* **19**: 82, 1926.

The second case was that of a man, aged 32, with definite signs of advanced urogenital tuberculosis. He also had a small stricture of the urethra which admitted only a filiform. In the process of dilatation acute miliary tuberculosis developed, from which the patient died.

The third case was that of peri-urethral phlegmon with sepsis. At operation it was found that tuberculosis of the urethra had been the primary lesion. Tuberculosis of the seminal vesicles was also found, this appeared to have developed more recently.

From these cases Richter concludes that tuberculosis of the urethra may become extensive without causing marked symptoms. For this reason, in any case of urogenital tuberculosis, one must bear in mind the possibility of tuberculous urethral stricture. Richter warns against the dilatation of tuberculous urethral strictures with sounds. He recommends operative exploration of the kidneys or ureters instead of cystoscopic investigation. He mentions further thirteen cases of urogenital tuberculosis with accompanying urethral strictures. In nine of these the primary focus was removed by nephrectomy, and in eight of the nine the urethral tuberculosis cleared up. Thus he concludes that urethral strictures of tuberculous origin should not be dilated with sounds, but should be treated by removing the primary focus, usually the kidney.

[ED. NOTE.—Tuberculous stricture of the urethra is an unusual lesion and is scarcely mentioned in textbooks on urology. When it does occur it is always secondary to genito-urinary tuberculosis elsewhere. For this reason one would assume that in many cases if the focus above the urethra, usually the kidney, is cleared up by operation, the urethra would tend to heal just as the bladder does. Thus Richter's conclusions seem logical and in accordance with accepted pathologic principles.]

Anomalies—Ritter⁶⁰ notes that there are but fifty-seven reported cases of double urethra. He reports a case in a boy, aged 2½, suffering from partial incontinence. Examination revealed a double urethra, one normal through the penis, and one an epispadic structure. The latter had no sphincter muscle, a condition which accounted for the incontinence. Treatment consisted of dilating the normal urethra and successful resection of the epispadic urethra. Histologic examination of the latter failed to reveal any evidence of sphincter muscle, but many nerve fibers were found. Ritter believes that the supernumerary urethra came from the same anlage as the normal urethra and that it grew out with the penis, but remained in communication with the bladder.

Baradulin⁶¹ noted thirty-nine cases of double urethra in the literature, three of which were reported by Russian observers (Koltchin

60 Ritter, O. Beitrag zur Kasuistik und Behandlung der durchgehenden, epispadischen Urethraverdoppelung, *Ztschr f urol Chir* 20 5, 1926.

61 Baradulin, G. Ein Fall von doppelter Urethra, *Urologia* 2 3, 1925, abstr., *Ztschr f urol Chir* 20 120, 1926.

Dedjurin, Fronstein) In Baradulin's case the extra urethra lay above the normal urethra, the separation being from 6 to 7 cm. from the external meatus. He cauterized the septum between the two channels to make a single passage.

Polyyps—Lloyd⁶² reports thirteen cases of urethral polyyps. They are frequently associated with chronic posterior urethritis and chronic prostatitis. This was noted in most of the cases reviewed. The chronic infectious process may be of long standing, preceding the formation of the polyyps by many years. The polyyps disappeared in one of Lloyd's cases after the patient had been suitably treated for prostatitis. The polyyps in most cases were situated at or near the orifices of the prostate or ejaculatory ducts, and in many instances showed evidence of an inflammatory origin. They resemble closely polyyps found in the nose, which are generally conceded to be due to inflammation. Lloyd believes that inflammation is responsible for most urethral polyyps. Treatment is generally ineffective, if the underlying disease in the prostate and vesicles is not treated at the same time.

TESTICLE

Tumors—According to Handfield-Jones⁶³ the gross appearance of chorionic carcinoma of the testicle depends largely on the amount of ordinary teratomatous tissue present. If a recognizable quantity is present, the picture will show typical signs, such as small cysts and areas of blue translucent cartilage. The area of chorionic carcinoma has the appearance of a blood clot. Plum-colored areas are seen practically homogeneous throughout except for small white friable areas of necrosis. The elements found in this type of carcinoma are brach: (1) syncytium, (2) Langhans' cells, (3) chorionic wandering cells, and (4) masses of blood and fibrin. These elements are described in detail.

Two types of tumor are noted. These are best described by Handfield-Jones as follows:

In the typical group the characteristics of the chorionic carcinoma appears in the first stage of gestation, are represented with regularity. They show well-developed continuous syncytial masses of protoplasmic strands and branching protoplasmic buds, and with a fine cellular ground work of numerous transparent polyhedral cells (the so-called Zellschicht (viz., Langhans' cells)).

In the atypical group, nearly everywhere the carcinoma is in the normal grouping and occurs only in isolated cells and small masses. The cell masses which form the surface and the nodules.

62 Lloyd, A. L. "A Clinical Study of Prostatitis and Its Relation to Chronic Prostatitis," *Ann. Surg.* 1925, Hosp. Rep. 75:234.

63 Handfield-Jones, R. M. "The Testis," *Brit. Med. J.* 1925, Report of New Clinical Trials, 13:20.

a hydatidiform mole may be taken as an example or pattern of these form. These cells rarely show the habitus of the delicate transparent, membranous, and often sharply circumscribed Zellschicht element with regular oval nuclei, frequent mitoses, and glycogenic cell protoplasm. More often they are compact, more deeply staining, and very irregularly shaped cells, with nuclei varying greatly in size, sometimes attaining properties, which allow the recognition of their syncytial character. These elements may form multinuclear aggregates, but in many cases no large syncytial masses occur.

Metastasis is common by the blood stream, but the lymphatics are also usually involved early and extensively.

In the present stage of knowledge of the origin of the teratomas, it is not possible to be assured of the finer details of their derivatives.

Treatment for Cancer —Roentgen-ray and radium treatment for diseases of the bladder and prostate is discussed in the Section on Urology of the Royal Society of Medicine. Finzi⁶⁴ outlines the methods of applying radium in the treatment of patients with diseases of the prostate and bladder. Large dosages are applied to the skin, about 500 millicuries. The urethral route is dangerous, as effective dosage would cause sloughing. The method of embedding radium in the prostate has been used extensively in Brussels. The radium in platinum needles is introduced through an incision in the perineum. The improvement in technic in recent years has consisted in the use of a number of needles instead of one or two large tubes, with the result that the irradiation is much more homogeneously distributed. The results in such cases are often satisfactory, and careful observation will be necessary to determine whether the results are as good as surgical procedures. In inoperable cases, the roentgen ray or radium or both, should always be tried. In cases of malignant disease of the bladder, operation should be performed, if possible. If not, it is worth while to irradiate, even as a palliative measure. Papilloma of the bladder should be treated by other methods, unless too much surface wall is involved.

Browne-Carthew⁶⁴ discussed the treatment of diseases of the prostate and bladder by applying radium through the rectum. He used 50 mg of the bromide of radium with an activity of 24,000 to 25,000 as measured and estimated in the Institut de Radium, Paris. The radium was in a tube which had been specially made for the treatment of a recurrent malignant lesion of the rectum. It had occurred to him that with this tube radium could easily be applied to the prostate and base of the bladder. He had had at one time under treatment and observation twelve or more patients with simple enlargement of the prostate. The patients had found that nocturnal frequency was diminished and that they passed a

⁶⁴ Finzi, N. S. Browne-Carthew, R. H. Morson, A. C., and Kidd, Frank. Discussion on Radiotherapy and X-ray Therapy in Diseases of the Bladder and Prostate. *Radiotherapy and X-ray Therapy in Diseases of the Bladder and Prostate*. 18 15, 1925.

better stream. In some of these cases, on palpation by way of the rectum the prostate seemed to have been softened by the treatment but such palpation was indefinite.

Morson⁶⁴ states that in malignancy of the prostate as in every other organ of the body, the only chance of eradication of the disease is by means of surgical intervention. He has been experimenting recently with a new electrical instrument on the lines of the cautery-punch of Young, but his treatment of tumors of the prostate by this means has been disappointing. In about 1 per cent of cases diathermy was of value. If the obstruction in the prostatic urethra was of fibrous tissue the use of this electrical treatment offered a more hopeful prognosis.

Kidd⁶⁴ states that tumor in the bladder and prostate is a local disease in its earliest manifestations. If seen by the surgeon early the best chance of cure is still to be obtained with the knife. Kidd feels that all improvements in the results of the modern operation on the prostate and bladder are not appreciated. He reports 129 cases of prostatectomy with only six deaths, twenty-one of thirty-five patients on whom subtotal cystectomy was performed for carcinoma of the bladder during the last fourteen years are apparently cured. He feels that the public is in danger of forgetting that operation can cure cancer in a fair proportion of cases. Physical agents, such as radium, the roentgen ray and diathermy should be considered as adjuvants to surgical methods, not substitutes.

Summarizing his cases, Kidd states that eight were cases of carcinoma of the prostate. Four were cases in which no operation of a radical type could be carried out. All four of these patients are dead. In none did the roentgen-ray treatment show a favorable effect and in two it appeared to make the patients ill and to hasten death. In three cases he removed what seemed to be simple benign growth of the prostate. Microscopic examination of the prostate showed early malignant changes. These three patients were exposed to the deep roentgen-ray treatment and are now alive and well. Nevertheless the results have not been better than in a considerable number of similar cases in which patients showing these early malignant changes were operated on for adenoma given the deep roentgen-ray treatment. Recurrence is possible in all these cases whether or not this treatment is carried out.

Kidd concludes that by deep roentgen-ray treatment the cure of cancer is accomplished in malignant disease of the prostate except in the advanced stage following operation. He believes that the early stages of carcinoma of the bladder are not destroyed by the roentgen-ray treatment. These seem to lose their lethal effect probably by becoming more resistant to the roentgen ray. Radium undoubtedly prolongs life for one or two years and may make the patient's life more comfortable. Radium may relieve or even cure prostatic hypertrophy.

It may be expected that deep roentgen-ray treatment will destroy a certain number of cancer cells. The vascularity of a tumor will be lessened, and the fibrous tissue around the tumor increased. The treatment also may produce a certain degree of active immunity. On the other hand, its immediate effect when applied over the abdomen is to cause protein shock, destruction of red blood corpuscles and depression of renal, suprarenal and hepatic function, which debilitated patients cannot incur without risk of life. If the treatment is persisted in too long it may render the cancer cells more resistant and even hasten metastasis, if it is too frequent or too intense it may produce severe, painful gangrene of the abdominal wall and sacral region. This occurred in 8 per cent of Kidd's cases.

According to Thomson-Walker,⁶⁵ tumors of the bladder are successfully removed by operation. In 119 cases of simple papilloma he employed transurethral electrocoagulation. None of the patients died and 74.4 per cent were free from recurrence for from one to eleven years. Operation (excision) was performed in 142 cases, with a mortality of 3.49 per cent, and 65.74 per cent were free from recurrence. In 126 cases of malignant growth in the wall of the bladder, resection was performed, the mortality was 6.34 per cent, and 66.3 per cent were free from recurrence. On the whole, the author was satisfied with the results, but in certain cases diathermy or operation failed, owing to the persistence or recurrence of the growth or because the measures were unsuitable in the advanced state of the growth, because of the septic or contracted state of the bladder, and disease of the kidney, or because of the feeble general state of the patient. Of the 491 cases of tumor of the bladder, 118 were unsuitable for radical operation, in most instances because of the extent of the growth. In view of the successful results obtained by irradiation elsewhere in the body, there seemed to be some prospect of success here also, but the author's experience in a few cases did not encourage him to hope that the surgeon would obtain assistance in operating from preparatory treatment by irradiation, rather, his opinion was the reverse. Neither were his experience and postoperative treatment of growths of the bladder, either by the gamma rays of radium or by hard roentgen rays, encouraging. He noted that mild urinary infection was sometimes converted into severe cystitis, and in other cases there was delayed healing of the wound or tendency of the wound to break down after such postoperative irradiation. His opinion was, therefore, that irradiation in the immediate postoperative stage was not suitable for growths in the bladder. If the growths were inoperable or if growths had recurred after operation, the result with hard roentgen rays was sufficiently encouraging to warrant a more extended trial. The

⁶⁵ Thomson-Walker, John. *Radiology in Urinary Surgery*, Brit. M. J. 1: 656, 1926.

only objection to irradiation in such cases is the local reaction but this does not counteract the good accomplished.

Thomson-Walker believes that radical operation for cancer of the prostate is too severe, and that irradiation is more satisfactory. Forty-eight of his patients who had carcinoma of the prostate were treated by hard roentgen rays. The treatment was carried out by twelve roentgenologists, seven of whom were in London; one patient was treated at Erlangen. General reaction was noted in eighteen of these cases; it was severe in seven. Local reaction occurred invariably, although it differed considerably in cases which otherwise appeared similar. At the time of the report twenty-four of the series of forty-eight patients were dead, four were seriously ill, nine were unchanged or slightly worse, six were improved, four were well, and of one there was no record. Eight of the twenty-four patients who died lived six months after the first exposure; seven patients lived from six to twelve months, six from twelve to eighteen months, two from eighteen months to two years, and one two years and seven months. The condition at the time of irradiation of the patients in this series and in those who remained seriously ill was advanced growth with the patient failing in twelve, large growth but general condition good in nine, and early growth and general condition good in seven. In forty-two of the forty-eight cases full notes were made of the changes in the prostate. In twenty-two, following irradiation, there was no decrease in size, hardness or fixity of the growth; in fifteen there was improvement which did not continue; and in five there was improvement which continued. The improvement in some of the cases was slight but in others pronounced. The hard prostatic mass appeared to melt away, and left only hard nodules, although after a period varying from two to six months the induration reappeared. In five cases, however, the growth disappeared entirely after irradiation. One of these patients, an old man, died six months after treatment from cardiac failure, but there was no recurrence of the growth. The other four survived and without recurrence the period since treatment being one, two, five and twenty-one, forty-one and forty-five months respectively. One of these cases was of rapidly growing endothelioma; the other four were of the ordinary scirrhous type.

Waters⁶⁶ states that the best treatment for superficial carcinoma of the bladder is a combination of deep roentgen rays and the application directly to the surface of the growth of the *radium*. The growth is destroyed by this method with minimal discomfort to the patient and no injury to bladder mucosa.

Infiltrating carcinoma is operable only in the early stages of the disease. Twenty-five per cent of the cases are operable.

⁶⁶Waters, C. A.: *Bladder Cancer*, 1924, p. 107.
 67Waters, C. A.: *Bladder Cancer*, 1924, p. 107.

were in situations that rendered them inoperable, or they were so extensive that radical removal was impossible. In such cases, when it is possible to apply radium directly to the growth, both radium and deep roentgen-ray therapy should be given a trial, for in a certain number of the cases favorable results can be obtained by this method alone. In cases in which this procedure does not yield the results hoped for, or in cases in which one feels that the growth is sufficiently localized to warrant implantations of radium needles, the bladder should be opened suprapubically, and screened radium needles implanted throughout the growth. If the growth is so extensive that a total of more than 2,500 mg hours is necessary, in order to destroy the cancerous areas thoroughly by implantations, this method should not be considered.

Tuberculosis—Ullmann⁶⁷ has noted results in forty-one cases of tuberculosis of the testicle, seminal vesicles and prostate treated with the roentgen ray since 1913. In most cases the disease was controlled. The success was questionable so far as the local process was concerned. No injurious results were noted. Some areas of induration were absorbed and fistulas closed. A number of patients died from general tuberculosis. Ullmann states that well localized growths, especially in the testicle, should be removed, and then roentgen-ray treatment should be given.

Diagnosis—Fryszman⁶⁸ believes that the cystoscope gives little information concerning the shape and form of diverticula. Because of the small field of cystoscopic vision, it is hard to estimate the size and shape of the stones. This information may be obtained from summing up numerous small fields, but even then only a relative idea is obtained. In some cases a simple roentgen-ray examination is of no value because the shadow of the stone overlies that of the spine. Fryszman has overcome this by making roentgenograms with his patients uniformly in the Trendelenburg position. In examination of diverticula, he used contrast cystography in the Trendelenburg position. In this position, the pressure of the adjacent organs is removed, and the true size of the diverticulum is demonstrated. In studying growths of the bladder he demonstrates what he terms "pneumocystography," which consists of placing the patient in the Trendelenburg position and inflating the bladder with air. He gives several illustrations which show fair results.

67 Ullmann K. Röntgentherapie bei der männlichen Genitaltuberkulose, *Wien med Wchnschr* **75** 2879, 1925.

68 Fryszman, Aleksander. Ein Beitrag zur Röntgendiagnostik der Blasensteine, Divertikel und Tumoren der Blase, *Ztschr f Urol* **20** 321, 1926.

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PERICARDIOTOMY FOR PYOPLERICARDIUM

REVIEW OF LITERATURE TO MAY 1927, AND REPORT OF FIVE
NEW CASES*

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According to Heyde, the ancients practiced pericardial incision but in the opinion of Burtenshaw, meagerness of the reports vitiates their acceptance as genuine examples of this operation. It is said that Golden removed the sternum and anterior wall of the pericardium from a soldier in whom a neglected wound of the chest had led to the development of a suppurative pericarditis and by this means obtained a cure. It is definitely known, however, that as early as 1648, Riolanus advised trephinement of the sternum for drainage of the pericardium. In 1818 Skielderup repeated Riolanus' suggestion, but it was not put into practice until 1855, when Malle evacuated a hemopericardium successfully through an opening in the sternum. The first and only instance of draining a pyopericardium by this route that we could locate in the literature is the case reported by Benman, in 1891, with recovery of his patient. Four of our patients were so treated, two were cured and two died.

Sénac, in 1794, recommended that the opening into the thorax should be made to the left of the sternum, but the operation was not attempted until 1798, when Desault endeavored to incise the pericardium in a case which had been diagnosed as pericarditis with effusion, but the condition proved to be a localized pleurisy situated in front of the pericardium.

The first successful incision of the pericardium was performed by Romero for serous pericarditis in 1819, in which time he reported six successes and one failure following open drainage between the fifth and sixth ribs on the left side.

The xiphocostal route was first described by Lericq in 1924, suggested to him by the case of a soldier in whom the pericardium was drained a stab wound in this region communicating with the pericardium.

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* Reprints will contain the following title: "Pericardiotomy for suppurative pericarditis."

The same approach was later proposed by Allingham and practiced by himself, Mintz and Rehn. Pendlebury has modified the method to the extent of resecting the sixth and seventh costal cartilages when it is thought necessary. In three cases of our series this method of approach was adopted, with two recoveries and one death. Of all the ways devised for doing pericardiotomy, either the transsternal or the subchondral route appears to be the best, of the two, the latter is preferable because it affords more space in which to work, insures a better exploration of the pericardial contents and provides drainage from the lower portion of the sac. Both may be performed with perfect satisfaction under local anesthesia.

To Hilsmann, in 1844, however, belongs the credit not only of being the first to perform pericardiotomy for pyopericardium, but also of being the first to cure a patient of purulent pericarditis by this means. Six years then elapsed before the operation was repeated by von Langenbeck, with an equally satisfactory result. The procedure was not undertaken again until 1879, when Rosenstein drained successfully the pericardial sac of a boy, aged 10, who was suffering with suppurative pericarditis, secondary to pleurisy. It was the report of Rosenstein, in 1881, concerning this case, that established surgical intervention as the proper treatment for purulent pericarditis. Less drastic measures had been thoroughly tried out and found wanting. Drugs had proved utterly worthless. Aspiration, though affording some temporary relief, invariably failed to save the life of the patient. Notwithstanding these examples of cures and the noteworthy statistical studies of Roberts (1897), Porter (1900), Eliot (1909), Rhodes (1915) and Poole (1921), pointing out the advantages of operative measures over therapeutic agents, the medical profession has been loath to advise drainage of the pericardial sac in the presence of pus, as the 118 cases collected from the literature by the authors of this paper bear silent but eloquent testimony. This antipathy toward pericardiotomy is indeed strange and hard to explain when contrasted with the directly opposite attitude adopted toward the management of suppurative peritonitis and empyema, in every way strikingly comparable conditions from the standpoint of therapeutics. The objects of this paper are, first, to add ten hitherto unpublished instances of pericardiotomy for pyopericardium to the literature and, second, to review the subject critically with the idea of bringing the history of surgical treatment of this malady up to date.

REPORTS OF CASES

CASE 1—A white boy, aged 4, entered the hospital on June 23, 1924. He was critically ill, having been sick a month with tonsillitis, otitis media and arthritis. His pulse was 160 and respiration 62; the face was deeply cyanosed, and his expression was anxious. The physical signs pointed to a pericardial effusion as the cause of the trouble, and the surmise was proved correct by the aspiration of 250 cc. of serosanguinopurulent fluid by a paracentesis pericardii. Cultures of

this fluid yielded a pneumococcus of no fixed type. Following the paracentesis the boy showed temporary improvement, but the next day his condition had grown so much worse that it was decided to perform a low transternal pericardiotomy under 0.5 per cent procaine hydrochloride anesthesia. This was easily accomplished by making a 4-inch (10 cm.) incision upward from the apex of the xiphoid cartilage in the midline of the chest. The incision was immediately deepened to the sternum, which was trephined with a Hudson burr just above the junction of the xiphoid process with the gladiolus, the site of the trephinement having been previously cleared of periosteum. The opening thus made in the sternum was enlarged with biting forceps. The posterior layer of the periosteum was now incised and the pericardium came immediately into view. It was tense, distended, grayish opaque and uncovered by pleura. The heart could be easily felt and was close to the pericardium. When the pericardium was incised 1 pint of seropurulent fluid escaped. Two Dakin tubes were placed along the right side of the heart and anchored to the skin by sutures. The mediastinum was protected with a sterile gauze tampon, and the wound in the skin closed down to the drains. The postoperative course was stormy. The boy's temperature gradually returned to normal, but his pulse continued rapid for a number of days. The edema disappeared almost immediately, and the respiration, though rapid, was fuller and deeper. The discharge from the pericardium continued to be profuse and after several days the pericardial sac was irrigated with gentian violet solution. He was discharged on July 12, 1924, and at present is in excellent health.

CASE 2—A white boy, aged 18, was admitted to the hospital on Jan. 27, 1925, for postgrippal pneumonia. When he was admitted, however, signs of pneumonia could not be made out, and after watching him for some time and having taken a number of roentgenograms of the thorax we diagnosed the condition as pericardial effusion. As the effusion was not large it was decided to perform a pericardiotomy without preliminary paracentesis pericardii. Accordingly on Jan. 30, 1925, a trephine opening was made in the lower end of the middle portion of the sternum under 0.5 per cent procaine hydrochloride anesthesia. The pericardium was not distended, but its parietal layer was thick and considerable difficulty was encountered in opening it because it was in intimate relationship with the heart. When the incision was made 150 cc. of seropurulent fluid escaped. The inner surface of the pericardium was somewhat shaggy. One small rubber tube was introduced into the pericardial sac along the right side of the heart and sutured in position. The patient was clinically all right on the second day. A culture of the blood was negative and the fluid removed from the pericardium did not show any organism in the smear. Inoculations of the fluid into guinea pigs gave negative results. The youth improved rapidly and on the twelfth day after the operation his temperature was normal. At midnight the pulse rate was 80 and the respirations were 22. He was discharged from the hospital on March 1, 1925, and is in excellent health since.

CASE 3—A white boy, aged 19, came to the hospital on Feb. 1, 1925, while in the medical service with pneumonia. He was given 0.5 per cent procaine hydrochloride anesthesia and a low transternal pericardiotomy was performed. The incision was made in the midline of the chest, 4 inches (10 cm.) long, and the sternum was trephined with a Hudson burr just above the junction of the xiphoid process with the gladiolus. The opening thus made in the sternum was enlarged with biting forceps. The posterior layer of the periosteum was now incised and the pericardium came immediately into view. It was tense, distended, grayish opaque and uncovered by pleura. The heart could be easily felt and was close to the pericardium. When the pericardium was incised 1 pint of seropurulent fluid escaped. Two Dakin tubes were placed along the right side of the heart and anchored to the skin by sutures. The mediastinum was protected with a sterile gauze tampon, and the wound in the skin closed down to the drains. The postoperative course was stormy. The boy's temperature gradually returned to normal, but his pulse continued rapid for a number of days. The edema disappeared almost immediately, and the respiration, though rapid, was fuller and deeper. The discharge from the pericardium continued to be profuse and after several days the pericardial sac was irrigated with gentian violet solution. He was discharged on July 12, 1924, and at present is in excellent health.

escaped. The patient's condition was desperate, and he survived the operation only a few hours.

CASE 4—A colored girl, aged 10, had been ill one week with influenza. When she was admitted to the hospital, she had a large pericardial effusion, and her condition was extremely grave. Paracentesis pericardii was not performed. Roentgen-ray examination of the chest showed both lungs clear and a large shadow in the cardiac region extending from well beyond the right margin of the sternum across the chest to a point outside the line of the left nipple. Pericardiotomy was performed by the transsternal route under local anesthesia. The girl failed to rally and died on April 4, 1925, the day following the operation.

CASE 5—A white man, aged 23, eleven days before admission to the hospital was taken sick with pneumonia. On the fifth day of his illness, the fever, which had begun to decline, suddenly rose, and his condition became alarming. When admitted into the hospital on Jan. 18, 1926, he was critically ill, he was dyspneic, the pulse rate was 160, and it was running, of small volume and paradoxical, the blood pressure was systolic, 100, diastolic, 60. The patient was somewhat cyanotic and had a slight cough, with practically no sputum. The left side of the chest was dull throughout. The right border of the heart extended almost to the line of the right nipple, the left merged with the general flatness of the left side of the chest. No heart sounds could be heard, but at the base of the sternum a pericardial friction rub could be distinctly made out. The abdomen was distended and tense, but not tender. A diagnosis of pericarditis with effusion was made. As the symptoms were urgent, it was decided to perform a pericardiotomy just as soon as the patient had had a few hours' rest. The operation was easily accomplished under 0.5 per cent procaine hydrochloride anesthesia. The pericardium was exposed by resecting the fifth, sixth and seventh left costal cartilages just lateral to the sternum. The internal mammary vessels were exposed and tied, and the pericardium readily came into view. On incising the pericardium, 2 ounces (62.2 Gm.) of thin pus escaped. The opening in the pericardial sac was enlarged, and a finger was introduced into it. No adhesions were felt. There was, however, a marked bulging inward of the left pericardial wall, which was tense. Two Dakin tubes were introduced into the pericardium, and the skin flap closed around these tubes. As a safeguard, the tubes were anchored to the skin by sutures.

A paracentesis of the left pleural cavity was performed, and 5,000 cc. of pus was withdrawn through the needle. This did not empty the pleural sac, but as the patient's condition was so grave, it was decided to do nothing further.

Following these procedures, the patient improved somewhat. His blood pressure rose to 120, and his pulse rate fell from 160 to 120. About fourteen hours after the pericardiotomy and paracentesis, a stab wound was made between the ribs, under local anesthesia, and a tube filled with water was inserted into the pleural cavity. The outer end of the tube was kept under water in a vessel beside the bed. This was done to prevent sucking, and during the next two hours, 3 quarts (143 liters) of pus drained from the left side of the chest. The patient's respiration was much relieved, but his general condition did not show improvement, and he died of exhaustion twenty-six hours following the pericardiotomy. A culture of the pericardial pus obtained at operation proved sterile.

CASE 6—This patient, a white girl, aged 9, was taken ill with sore throat two weeks before operation. She was apparently making a good recovery when she suddenly developed severe pain in the abdomen. The condition was diagnosed as appendicitis, but on admission of the patient into the hospital, the diagnosis was changed to pneumonia. One week later, or two weeks from the onset of the

shaggy and rough. Four ounces (124.4 Gm) of serohemorrhagic fluid was liberated, which, on bacteriologic examination, showed pneumococcus. The edges of the pericardial incision were sutured to the lips of the subcutaneous wound, and a raw gauze tampon was introduced into the sac. The postoperative course was fairly stormy, the discharge soon changed to a thick, grumose pus, and the temperature, pulse and respirations did not reach normal both morning and night until February 8. From that time on the patient made an uninterrupted recovery and was discharged on March 16, 1927, as completely cured.

CASE 8—A young colored man was admitted to the hospital on May 18, 1920, with pneumonia of the left upper lobe of a week's duration. Though the pneumonic process cleared up promptly, the patient continued to run a mild fever of obscure origin, accompanied by an accelerated pulse and rapid respirations. On June 5, 1920, roentgen-ray examination revealed a large, sharply defined shadow in the center of the chest, which was taken for a mediastinal abscess located in front of the heart. However, on June 7, a purulent pericardial effusion was suspected. Aspiration in the right fifth intercostal space, close to the sternum, recovered thick, greenish pus, from which the pneumococcus, type 4, was cultured, thus confirming the clinical impression of pyopericardium. An operation was performed on June 7, 1920, by Holland, under 0.5 per cent procaine hydrochloride anesthesia. The pericardial sac was approached through the right fifth interspace by 5-inch (12.7 cm) incision. The right pleura was accidentally opened. It did not contain pus, but on the introduction of a finger into the opening a hard bulging mass was felt, which beat synchronously with the heart. A small hypodermic needle was inserted into the swelling, and pus was obtained. The pericardial sac was then incised, and 1 quart (4.3 liters) of thick, greenish pus escaped. A small rubber tube was placed in the pericardial cavity, and several gauze wicks were introduced to seal the pleural cavity. The postoperative course was smooth. The patient improved steadily and rapidly. The opening in the pericardium had closed on June 19, and the man was discharged from the hospital on June 24, 1920, in excellent condition.

CASE 9—A white girl, aged 8, was admitted to the hospital on Nov. 18, 1925, for pain and tenderness in the left hip and in both wrists. Three weeks previously, she had had a small sore on the left heel, which had healed under treatment with home remedies. Ten days before, her left leg had begun to hurt, and for four days she had complained of chilly sensations, but had not had a definite chill. When she was admitted the pulse rate was 150, the respirations, 30, the temperature, 103 F. The leukocytes numbered 21,000, with a polymorphonuclear count of 80. The lungs and heart were normal. Roentgen-ray examination failed to disclose any disease of the bone or periosteum. As early as November 21, a staphylococcus was isolated from the blood stream. On November 24, an alternating friction murmur was detected at the base of the heart. The course was gradually but steadily downward. On November 29, the child's condition was so desperate that an intravenous injection of gentian violet was made, without any material benefit. On December 4, a roentgenogram of the chest showed a markedly enlarged cardiac shadow, which suggested a pericardial effusion. This impression was confirmed by the insertion into the pericardium of an aspirating needle through the left fifth space, with the liberation of pus, which yielded *Staphylococcus hemolyticus* on culture.

The operation was performed on Dec. 6, 1925, by Linn under ether anesthesia by removing 1 inch (2.5 cm) of the left fifth costal cartilage. The pericardium, which was easily recognized, was incised, and a large amount of sanguinopurulent fluid was released. This pus yielded *Staphylococcus hemolyticus* in pure culture.

In cases 8 and 10, the pericardium was reached from the right side, once by resecting the fifth costal cartilage and on the other occasion through the fifth interspace. This route was selected in case 10, because the left side in front was resonant throughout. The pleura was opened in both of these cases without any untoward effects.

In case 9, the left fifth costal cartilage was resected.

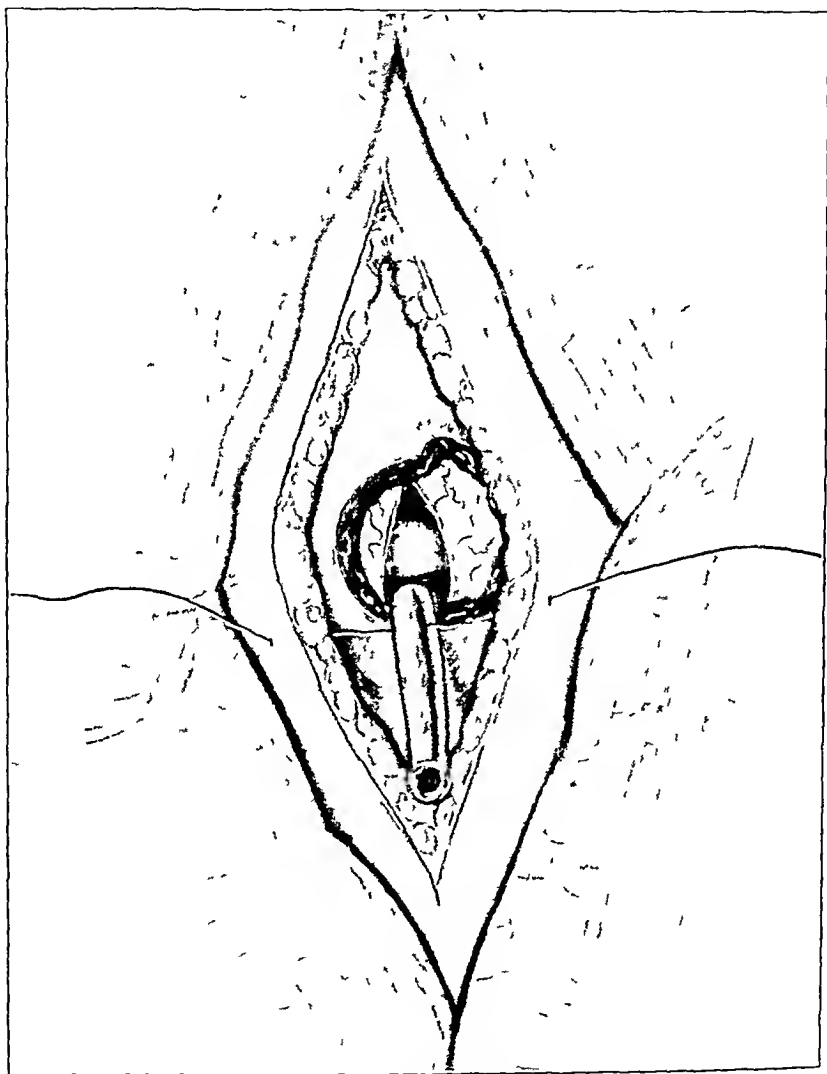


Fig 2—Drainage tube sutured in position after pericardiotomy by the sternal route

In every instance the pericardium was thick and taut, and the heart seemed close to the anterior pericardial wall, so close that it gave the impression that there was no fluid in the pericardial sac. Several times it was difficult to grasp the pericardium with toothed forceps, in which event a small hook was found satisfactory. The pericardium is easily recognized because it is gray, thick and opaque. It differs markedly from the pleura, which is thin and translucent.

If the transsternal route is chosen, care should be exercised not to make the opening too high, as this will expose the pericardium close to where it is reflected from the large vessels. The space here between the two layers of the pericardium is narrow, and drainage is not so satisfactory.

Though purulent pericarditis is not a rare lesion, and operation offers the patient his best if not his only chance we could assemble but 128

TABLE 1—*Etiology of Pericardial Effusion*

	Recovered	Died	Not Stated	Total
Pneumonia	18	14	0	32
Measle and pneumonia	1	0	0	1
Tonsillitis and pneumonia	1	0	0	1
Influenza and pneumonia	5	0	0	5
Pneumonia and pleurisy	2	0	0	2
Pneumonia and empyema	2	7	0	9
Influenza pneumonia and empyema	0	1	0	1
Measle pneumonia and empyema	1	0	0	1
Tonsillitis pneumonia and empyema	0	1	0	1
Measles pneumonia pleurisy and empyema	1	0	0	1
Abscess pneumonia pleurisy and empyema	0	1	0	1
Empyema	2	2	0	4
Measles and empyema	1	0	0	1
Influenza and empyema	0	1	0	1
Tonsillitis and empyema	0	1	0	1
Nasal sinusitis and empyema	0	1	0	1
Pleurisy	1	2	0	3
Abscess pleurisy and pyemia	1	0	0	1
Tonsillitis pleurisy and arthritis	1	0	0	1
Pyogenic sepsis and pleurisy	1	0	0	1
Tonsillitis and pleurisy	1	0	0	1
Pulmonary gangrene	0	1	0	1
Typhoid fever and congested lungs	0	1	0	1
Appendicitis () with pneumococcus in pericardial exudate	1	0	0	1
Whooping cough	0	1	0	1
Influenza	2	3	0	5
Osteomyelitis	5	8	1	14
Osteomyelitis empyema pneumonia and sepsis	0	1	0	1
Pyemia	1	4	0	5
Gunshot and stab wounds	12	0	0	12
Idiopathic	2	1	0	3
None given	4	3	0	7
Primary mediastinitis	0	1	0	1
Esophageal perforation	0	1	0	1
Gangrene of feet	1	0	0	1
Trauma to chest	1	0	0	1
Rheumatism	2	0	0	2
Tonsillitis, otitis media and arthritis	1	0	0	1
Total	71	56	1	128

instances of operative relief of the condition, of which number, 118 were gathered from the literature. In analyzing these cases, we find ninety-three operations were performed on men and twenty-seven on women, in eight cases, sex was not mentioned, thus giving a preponderance of men in the ratio of $3\frac{1}{2}$ to 1.

Thirty-one were between 1 and 10 years of age, thirty-eight between 10 and 20 years of age, twenty-five between 20 and 30 years of age, fourteen between 30 and 40 years of age, four between 40 and 50 years of age, and one was between 50 and 60 years of age. In fifteen cases the age was not specified. Three of these patients were described as men, five, as soldiers and one, as a boy, six were not described at all.

Ninety-four were under 30, and sixty-nine were below 20 years of age. The largest proportion of these patients seen by the surgeon are under 30 years of age. The youngest patient subjected to operation was 1¾ years old, and the eldest, 56.

Only three cases were classified as idiopathic. In one of these, the pneumococcus was recovered from the pus removed by aspiration prior to operation, and in another a varied and numerous bacterial flora was recovered. In twelve, it was caused by the direct implantation of pyogenic organisms introduced from without by bullet or knife wounds.

TABLE 2—Results of Bacteriologic Examination

	Recovered	Died	Total
Pneumococcus	12	9	21
Pneumococcus, type 1	1	0	1
Pneumococcus, type 4	2	0	2
Pneumococcus, no fixed type	1	0	1
Pneumococcus, type 4, later streptococcus hemolyticus, staphylococcus albus, gram negative, nonmotile, nonliquefying bacillus and diphtheroid bacillus	1	0	1
Pneumococcus from empyema at autopsy	0	1	1
Pneumococcus in pus complicating so-called case of appendicitis	1	0	1
Streptococcus	8	2	10
Streptococcus, Staphylococcus aureus, also bacilli	0	1	1
Streptococcus nonhemolyticus from empyema, also staphylococcus pyogenes aureus, the latter probably a contaminator	1	0	1
Streptococcus and staphylococcus at autopsy	0	1	1
Staphylococcus	0	1	1
Diplococci of staphylococcus form, staphylococcus pyogenes albus from the blood stream	0	1	1
Staphylococcus hemolyticus	0	1	1
Staphylococcus pyogenes albus	1	0	1
Staphylococcus	3	2	5
Staphylococcus	1	0	1
Staphylococcus	0	1	1
Staphylococcus, next day rod shaped bacteria	0	1	1
Staphylococcus, B. perfringens, enterococcus	1	0	1
Colon bacillus	1	0	1
Double coccus not considered pneumococcus	0	1	1
Bacterial flora varied	0	1	1
Short bacillus, next day B. pyocyaneus	1	0	1
Rod shaped bacteria, neither pneumococci nor streptococci	0	1	1
Rod shaped bacteria	1	0	1
No organisms in smear, mouse inoculation sterile	1	0	1
Pus sterile	1	0	1
Total	38	24	62

In seven, the article gave no clue to the source of infection. In a few, the pericardial disease resulted from an extension of an inflammatory process in adjacent structures directly into the pericardium. In the majority of instances, however, the pyopericardium was attributed to a metastasis from a distant focus of infection. Osteomyelitis and pyemia were responsible for twenty of these cases, and diseases of the respiratory tract accounted for seventy-five. Of great interest in this connection was the incidence of pneumonia and empyema, either alone or in combination as a coincidental, primary or secondary process, one or the other or both having been noted in fifty-one cases.

Bacteriologic Examination—Bacteriologic examination of the pus was made in sixty-two of these cases. In two instances, the exudate was sterile. In one case the colon bacillus was responsible for the con-

dition. It had been introduced from without through a stab wound, however. A scattering of other organisms was mentioned, such as *B. pyocyanus* and *B. pertingens*, but the chief offenders were the pneumococcus twenty-eight times, the streptococcus, thirteen times and the staphylococcus thirteen times. Death occurred in 37.03 per cent of the purulent pneumococcal pericarditic group, in 30.8 per cent of the streptococcal and in 53.8 per cent of the staphylococcal. Although it is not safe

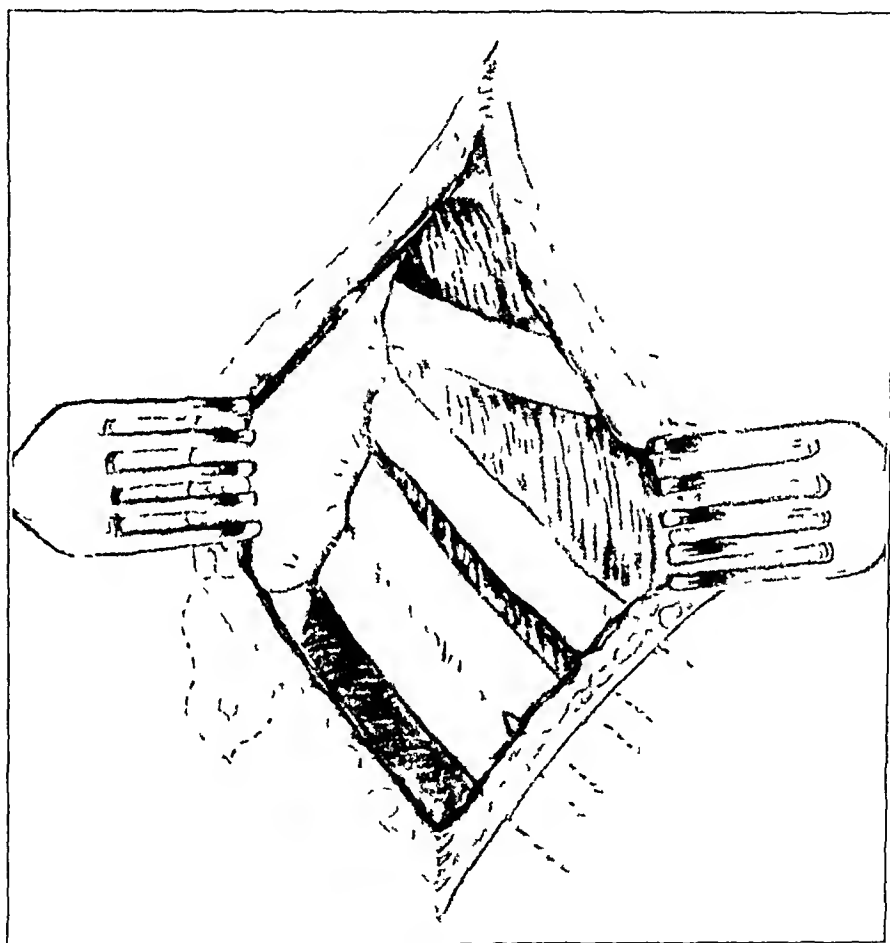


Fig. 3.—First stage in the xiphocostal approach for pericardiotomy

to generalize from such a small series, these observations seem to indicate that the staphylococcal infection is the most deadly of the three.

Paracentesis—Diagnostic puncture was practiced on eighty-six patients, without injury to the internal mammary artery to the peritoneum or to the heart. Occasionally the pleura was traversed. In fifteen cases diagnostic puncture was not attempted, and in twenty-seven instances the report failed to mention whether the procedure was employed or not.

The sites usually elected for puncture were the left interspaces near the sternum from the second to the seventh inclusive, more rarely the left fifth and sixth spaces just within the outer limits of pericardial dullness, the left costoxiphoid angle, the subxiphoid route, the right fourth and fifth spaces near the sternum and the right chondroxiphoid region. Occasionally the patient was tapped more than once, for either diagnostic or therapeutic purposes, but the latter invariably failed to render lasting benefit. On the other hand, many authorities condemn the use of the aspiration needle, first, as being too hazardous, and second, as unnecessary for making a correct diagnosis in the presence of the characteristic physical signs and roentgenographic evidence. If in doubt as to the nature of the disease, it is much safer, they claim, to cut down onto the pericardium and to enter this structure under direct vision rather than to jab a needle blindly into the chest with the possibility of entering the pleural cavity and thus instituting an empyema or of puncturing the heart and causing the death of the patient from hemorrhage. While there are numerous instances on record in which the heart has been punctured during an attempt to aspirate the pericardium, fortunately the accident is relatively uncommon, and, if it does occur, is ordinarily quite innocuous, but it may prove fatal (West). When a paracentesis pericardii has been definitely decided on, if pus is suspected, Pincoffs cautions that the needle should be introduced close to the sternum through the lowest possible interspace on the left side, with its point directed slightly downward and laterally so as to parallel the ventricles. Another strong objection to paracentesis is the obtaining of a dry tap, even in the presence of pus. Among others, Coultts had this experience, which tended to upset a diagnosis otherwise well established and made him hesitate momentarily about sanctioning operative relief.

Aspiration is valuable only when fluid is liberated, but, as has already been intimated, it may prove a hindrance rather than an asset. In this connection, the question as to the situation of the heart when the pericardium is more or less full of fluid is of some moment. Brentano, from his clinical experience, declares that in all pericardial effusions the heart lies most often right against the anterior wall of the sac even if adhesions are not present, and that in many cases there will be a fusion between the pericardium and the anterior wall of the heart. This means that the heart is generally in a position easily reached by the needle and likely to be punctured unless excessive care is exercised when the needle is introduced. On the other hand, when aspiration fails to disclose the expected pus, if the clinical signs indicate its presence, adequate surgical measures should be promptly initiated for as a rule the pericardial fluid lies behind the heart and is therefore out of reach.

Pus—The amount of pus varied from a few drops to as much as 7 500 cc. Often the exudate was under high pressure and was described

on occasion as fetid, blood-stained, thin, turbid, thick, bright green, grayish yellow creamy, inoffensive or cloudy. In the large proportion of instances, it had collected behind the heart and had pushed this organ forward directly against the anterior pericardial wall. In a few of the cases, the heart was attached to the pericardium by firm adhesions. Usually it was closely approximated to the pericardium, but on rare occasions a thin layer of pus was found interposed between these struc-

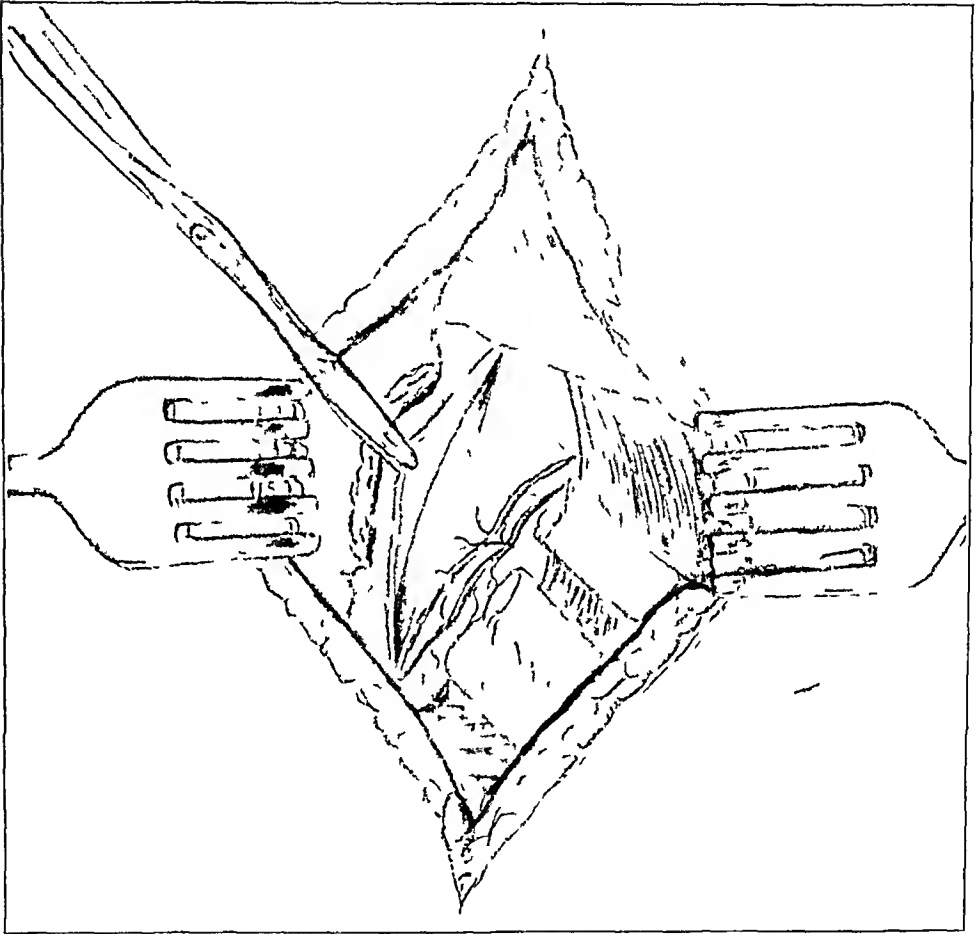


Fig 4—Incision into the pericardium through the xiphocostal route

tures. For this reason, paracentesis is inadvisable, as there is considerable danger of injuring the heart. In four cases of this series, the fluid evacuated was potentially purulent, for it contained pyogenic organisms, and the discharge promptly changed to pus soon after drainage was established.

Diagnosis—The question of a correct diagnosis depends largely on a recognition of those diseases in which pyopericardium is a complication. Then with a careful routine examination of the chest when the

patient is not doing well, supplemented by a roentgenographic examination of the thoracic viscera and, if deemed necessary, by a paracentesis pericardii, difficulty should not be experienced in arriving at a proper conclusion. In this series of 128 cases, diagnosis was made before operation in 116 instances, in two after opening the chest for the evacuation of a supposed pleural exudate, and in ten the time of diagnosis was not mentioned. Osler states that in spite of the clear-cut clinical picture, probably no other serious lesion is so frequently overlooked. In this connection, it is interesting to note that Stone found purulent pericarditis in forty-four, or 14.5 per cent of 300 autopsies performed on patients who died of pneumonia, none of whom had been operated on. A diagnosis apparently had not been made in any of these cases. Barkan and Lucas have gathered from a total of 3,248 autopsies, made at the Harvard Medical School from 1896 to 1911, six cases of suppurative pericarditis, of 324 cases of all types of pericarditis, Cowan discovered at necropsy twenty-four instances of the suppurative variety. In the cases of Craig and Mann, the abdominal symptoms so simulated an attack of appendicitis that the malady with which they were dealing was at first thus interpreted. One of the patients in our series was sent to the hospital by the attending physician under this impression. Fortunately, the error was soon recognized, and with the institution of proper medical measures, no damage resulted from the mistake.

Primary Operative Results—Of the 128 cases herein collected, seventy-one patients, or 55.47 per cent, recovered, fifty-six, or 43.65 per cent, died, and in one case, or 0.78 per cent, the outcome was not mentioned. According to Rhodes, the death rate in patients not operated on or treated by aspiration alone is 100 per cent, and under similar circumstances Pincoffs estimates a mortality of well above 70 per cent for the purulent pneumococcic group. By comparison of these figures, the superiority of pericardiotomy is indisputable in that it offers a salvage of at least 50 per cent against, at best, only sporadic cases of recovery by other kinds of treatment.

A resection of a rib or costal cartilage was made in seventy-one cases. Of this number, forty-two, or 60 per cent, of the patients recovered, and twenty-eight, or 40 per cent, died. According to the preference of the surgeon, from the third to the eighth rib on the left side and the fourth and fifth ribs on the right were selected for this purpose, but the left fifth was the one commonly chosen. The approach was made through an intercostal space in thirty-nine cases, with nineteen, or 48.7 per cent cures and twenty, or 51.3 per cent, deaths. Of the remaining nineteen cases five operations were performed by the transsternal route, with three cures and two deaths, one by a trap door, with recovery, two by incision at first and later a resection with cures, one by incision through skin insertion of a trocar and the institution of continuous suc-

tion, with recovery, in nine operations which were not described, three patients recovered and five died and in one case the result was not given. On the whole, it would appear from these figures that pericardiotomy through the resection of a rib is a slightly better procedure than through an intercostal space. At any rate, by affording more room, it adds greatly to the comfort of the surgeon and lessens rather than increases the operative hazards.

The question of recovery seems, however, to depend more on the etiology of the lesion than on the method by which the pericardium is attacked. There were twelve cases of gunshot or stab wounds, with 100 per cent cures, fifty of pneumonia, with 50 per cent cures, seventy-five of respiratory lesions, with 49.3 per cent cures, eight of pyemia, with 37.5 per cent cures, and fifteen cases in the osteomyelitic group, with 33.33 per cent cures.

Symptomatology—Those interested in this phase of the subject should consult the table with abstracted case reports. Therein will be found in sufficient detail the subjective and objective observations as recorded in the original sources. According to this table, enlargement of the area of precordial dulness occurred ninety times, rapid pulse, fifty-nine times, quickened respiration, forty-one times, distant and weak heart sounds, fifty times, elevated temperature, fifty-eight times, normal temperature, six times, inaudible heart sounds, seven times, paradoxical pulse, ten times, enlarged and displaced liver, sixteen times, epigastric tenderness and pain, fifteen times, apex beat not palpable, twenty-four times, bulging precordium, eleven times, dyspnea, fifty times, cyanosis, either local or general, forty times, friction rub, twenty-six times, absence of friction murmur, eleven times and leukocytosis, thirteen times.

Many of the case reports are meager, however, therefore, they are of little value for statistical purposes. Of particular interest clinically is the occasional absence of fever (Speed, Stoker, McConnell). Not much reliance can be placed on the presence of the friction murmur, as it is fleeting and has often disappeared, if it has been present, before the examination of the patient has been made. In spite of a large effusion, it was noted by Gluck in one of his cases. Of the utmost value is the bottle-shaped roentgenographic shadow in the center of the chest. The roentgen ray was first used for this purpose by Napalokow on March 7, 1902. It is mentioned as having been employed in thirty of the cases comprising this series.

Open drainage at the earliest possible moment, as advocated by Gaston, appears to be the best way of handling this malady. Unfortunately, a careful analysis of the material available is not in accordance with this view, for of the ninety-six patients operated on within from a few days to eight months after the diagnosis was made, fifty-six, or 58.47 per cent,

recovered and forty, or 41.6 per cent, died, of thirty-six patients operated on within a few days, twenty, or 55.5 per cent, recovered and sixteen, or 44.5 per cent, died, of sixty-one patients operated on within less than two weeks, thirty-four, or 55.7 per cent, recovered and twenty-seven, or 44.3 per cent, died, of seventy-eight patients operated on within two weeks, forty-five, or 57.5 per cent, recovered and thirty-three, or 42.3 per cent, died, of eighteen patients operated on after two weeks, eleven, or 61.1 per cent, recovered and seven, or 38.9 per cent, died

Regardless of the time which has elapsed between the diagnosis and the operation, the proportion of cures maintains a fairly uniform level. Some factor other than early operation must, therefore, be the determining influence as to whether the patient is to live or to die. In this connection, however, Klose and Strauss voice the opinion that it is best to operate before the exudate has changed to pus. They claim that suppurative pericarditis may be prevented, even in the presence of pyogenic organisms, if such a policy is adopted, and they furnish as substantiating evidence a patient treated by them in this manner with success. The experience of Brooke¹ would seem to support this contention. Thirty-six cases of pericarditis secondary to osteomyelitis have been recorded, he says, in which drainage of the pericardium was performed. Recovery after operation took place in two instances only. He attributes this high mortality to delay in operative intervention. For example, in twenty of the thirty-six cases, pericardiectomy was performed from three to ten days after the fluid in the pericardium had been definitely diagnosed clinically. A good illustration of this is seen in the case of the child who was admitted into the hospital with an acute osteomyelitis of the left femur, for which immediate operation was performed. Eight days later, the boy did not show any signs of improvement, and examination of the chest revealed the presence of a pericardial effusion, for which paracentesis was performed. Turbid serum was drawn off, but at the end of forty-eight hours micro-organisms were not found. Ten days later, the pericardium was again aspirated. This time pus teeming with *Staphylococcus pyogenes-aureus* was obtained. Pericardiectomy followed, with death twenty-four hours later. Other pyemic foci were not found at autopsy. The other examples are all similar in that the pericardiectomy was delayed until puncture of the pericardium revealed a purulent change in the pericardial fluid. The records of the two cases in which recovery ensued are here given. Both patients were operated on while the exudate was still turbid.

1 We have not included any of Brooke's cases in the tabulated list of pericardiectomies because the author has failed to state whether they were collected from the literature or were original observations. From the contents of the article it was impossible for us to decide this question and rather than to duplicate cases, we give them in a supplementary table.

A boy, aged 11 had osteomyelitis of the right tibia. An operation was performed immediately. Eight days later, the patient's condition was much the same and for the first time a pericardial rub was heard. On the third day, it had disappeared, and there were definite signs of fluid in the pericardium. On the twelfth day after admission, the cardiac area was enlarged both to the right and to the left. The pericardium was tapped, and a slightly turbid fluid was drawn off. As this was thought to contain pus, an immediate pericardiotomy followed, subsequent bacteriologic examination of the fluid demonstrated the surprising fact that it was sterile. Twelve hours afterward the wound was discharging pus containing a rich growth of *Staphylococcus pyogenes-aureus*. Three months later, the boy was capable of doing a fair amount of exercise. No signs of adherent pericardium were present.

The second patient, a boy, G. H., aged 12, was admitted to the hospital for an acute osteomyelitis of the left tibia, and operation followed promptly. Subsequently further osseous foci developed and were incised and drained. On the twenty-eighth day after the boy was admitted, a distinct rub was heard over the heart; it disappeared six hours later. Meanwhile the limits of cardiac dulness were extending, and signs of pericardial fluid were well marked. Twelve hours later, a needle was inserted in the pericardium, and a slightly turbid fluid was withdrawn which proved to be sterile. At the time, the exudate was thought to be infected, and pericardiotomy was performed, a rubber tube being left in situ. Four days after the operation, the fluid escaping from the drainage tube was distinctly purulent, and when examined microscopically it revealed *Staphylococcus pyogenes-aureus*. At the time of the report, the boy was recovering rapidly, he was up and walking about the ward and had no signs of adhesive pericarditis.

In case 7 of our series, the fluid was serohemorrhagic, and the patient recovered satisfactorily.

Here, then, are four cases in which the exudate was infected but nonpurulent, and in which all the patients recovered. The question naturally arises, should this be the line of treatment invariably pursued in cases of exudative pericarditis potentially purulent? The evidence seems to be in favor of such treatment, but the answer to the problem must await further experience. These are desperate cases, and anything that holds the promise of a lessened death rate should be given an extended trial before it is rejected.

Our investigations would lead us to believe that after the exudate has become distinctly purulent a reasonable delay does not compromise materially the chances of recovery. When the disease has become fully established, it would appear that the only hope for lessening the mortality rate is the early recognition and prompt evacuation of attendant purulent foci. No matter how well or at what stage pericardiotomy is performed, it fails to succor if an abscess in the pleural cavity is overlooked, or if secondary collections of pus in the pericardial sac escape detection. Occasionally a second intervention may be found necessary to relieve a pocketing of the pus, for better drainage or to prevent blocking of the drainage tube. Of the 128 cases collected herein, this happened in eleven, namely, once each in cases reported by Porter,

Ljunggren, Byles, Peters, LeConte, Pool, Wood and Bradley, Lynn, Winslow and Shipley, Quincke and Halsted, with six recoveries and five deaths. Porter, Ljunggren and Quincke first obtained drainage in their cases by an intercostal incision, then some time later were compelled to resect a rib to obtain better drainage. Peters made an intercostal incision which had to be repeated two days later, because the drainage tube had become blocked. LeConte had the same experience. Wood and Bradley, Pool, Lynn, and Winslow and Shipley reopened the wound, inserted a finger and released some reaccumulated pus. Byles incised down to the pericardium and aspirated some pure blood. Then he closed the wound, but he reopened it later, incised the pericardium and evacuated pus. As his patient was not doing well, Halsted introduced a finger into the pericardium, but could not detect any reaccumulation of pus.

On occasions, though fortunately rare, the heart has been noticed to cease beating as the pericardium is incised. This peculiar phenomenon, spoken of as cardiac "still-stand," has occurred in cases reported by Harrigan, Metivet and Ljunggren. In Harrigan's case, the temporary arrest of the heart was relieved by the placing of drains, but the heart stopped permanently four days thereafter. Metivet had a strikingly similar experience. With the injection of epinephrine into the cardiac musculature, pulsation returned, but ceased permanently in half an hour. Ljunggren also reports a heartblock which behaved precisely like those in the preceding two cases. The heart lay motionless in its sac, but on compression of the left ventricle it began to pulsate again. A year later the patient was alive, with the area of cardiac dulness within normal limits. More than one instance is recorded in which an incision or puncture evacuated the pericardial effusion into or through the left pleural cavity. In some cases a thoracotomy was performed for a supposed pleural exudate, but a distended pericardium was found to exist and was then tapped through the original wound. West, Savory, Lane, and Steward and Garrod have recorded cases illustrative of this mistake.

While the closed method for withdrawing a pericardial exudate, as devised, described and practiced successfully by Whittemore, may not come strictly under the category of a pericardiectomy, it is nevertheless akin to that procedure, in that the surgeon exposed the pericardium through an open incision before puncturing the wall of the sac. It is applicable only before large masses of fibrin have formed, otherwise some one of the open procedures must be employed.

The presence of an empyema was diagnosed in sixteen patients, of whom seven recovered and nine died following thoracotomy. On eight occasions this complication was overlooked entirely and was not suspected until autopsy. It is only reasonable to assume that a few patients

in the latter group would also have recovered, if they had had the advantages of a pleural damage

Six of the patients developed pleurisy with effusion, in three of whom the condition was found at autopsy. Of the remaining three, two recovered and one died.

Secondary Operative Results—Operative intervention for pyopericardium has been condemned as unwarranted on the grounds that if the patient escapes with his life he will sooner or later develop a fatal

TABLE 3—*Pleural Complications Empyema*

Case No	Side	Operated on	Discovered at Autopsy	Recovered	Died
3	Left	Yes		Yes	
11	Right	No	Yes		Yes
12	Left	No			Yes
21	Bilateral	No	Yes		Yes
26	Left	Yes			Yes
27	Left	Yes			Yes
33	Left	Yes			Yes
35	Left	Yes		Yes	
42	Bilateral	Yes			Yes
48	Left	No	Yes		Yes
54	Right	Yes			Yes
58	Left	Yes		Yes	
64	Left	Yes			Yes
66	Right	No	Yes		Yes
73	Left	No	Yes		Yes
81	Right	Yes			Yes
82		Yes			Yes
91	Left	No	Yes		Yes
92		Yes		Yes	
96	Left	No	Yes		Yes
110	Right	Yes		Yes	
116	Left	Yes		Yes	
121	Right	Yes		Yes	
123	Left	Yes			Yes
24		16	7	7	17

Case No	Pleurisy Side Tipped and Times	Discovered at Autopsy	Recovered	Died
7	Right	Yes		Yes
8	Left	Yes		Yes
10	Right	Yes		Yes
13	Left		Yes	
112	Left	Yes		Yes
115			Yes	
6	2	3	2	4

obliterative pericarditis. In such cases death is delayed but not stayed, and life is prolonged only for a shorter or longer period at the expense of a crippling invalidism, unless the patient is relieved by cardiolysis, a dangerous procedure in itself and as yet too recent a development to have established its real status. Fortunately, twenty-nine cases are available in this series which throw considerable light on this phase of the subject. Instead of supporting the commonly accepted opinion that adherent pericardium is an inevitable consequence, they appear to supply ample proof to the contrary. In all of these cases, at least five months had elapsed since the operation, and in one as long as twenty-one years had supervened. Our investigation shows that twenty-five of

these patients were alive, well and at their usual vocation at the time of the report, with their cardiac boundaries within normal limits. One was still alive, but had developed an adhesive pericarditis, and his death was momentarily expected (Davis). Of the three remaining patients, one had died three years after the pericardiotomy, but as the patient had passed from the care of the operator, the cause of death could not be

TABLE 4—*History of Patients Living Five Months or More*

Time	Case No	Comment
5 months	9	**
	41	Moderate degree of cardiac hypertrophy, but no signs of adhesive pericarditis
6 months	20	In excellent health and attending school, no symptoms referable to heart or lungs
	67	At work
8 months	109	Capable of any task, even the most laborious
	110	In normal health and able to exercise without embarrassment
1 year	31	Quite well and at work
	35	In excellent health
	37	Area of cardiac dullness within normal limits
	53	Alive and in good health
	58	Could play as well as ever
	63	Well and doing light work, no dyspnea, no retraction of interspaces over or behind cardiac area, outline of cardiac dullness normal, apex beat in fifth space within midclavicular line, no venous pulsation in neck, no signs of adhesive pericarditis
	80	Died of a recurrence of an abscess of the brain
	98	On roentgen ray examination, heart boundaries were normal with systolic retraction of precordial region except at the apex, where a positive pulsation was seen just inside left nipple line, absolute cardiac dullness, left border showed a mitral configuration, right border not demonstrable. This meant adhesive pericarditis was in association with chronic mediastinitis and fusion of pericardium with pleura to wall of the chest. Author says that this is an excellent example of postoperative result, which shows why the prognosis is unfavorable.
2 years	117	In good health, scar retracted slightly with each systole, no retraction at apex
	124	In excellent health
	22	Heart in normal limits, patient well
	32	Was enjoying good health
3 years	38	Heart normal
	120	In excellent health
	30	Died 3 years later, but author did not know cause of death
3½ years	119	In excellent health
8 years	29	No retraction of spaces with systole, heart sounds normal
9 years	5	Perfectly well, no signs of adhesive pericarditis, had been for years in active work and was capable of any ordinary muscular effort
	56	Entirely well
21 years	65	Heart in its normal limits, its tone full and pure, pulse regular
Not stated	49	In good health
	114	Died later of adhesive pericarditis

ascertained (Eiselsberg), one had died of abscess of the brain a year later (Johnson in Godlee) and one of adhesive pericarditis (Darrach).

Thus only two, or 7 per cent, of twenty-nine patients had developed intrapericardial adhesions in such a degree as to cause baneful symptoms. In the light of these observations, it would appear that the occurrence of adhesive pericarditis is not as common as heretofore supposed.

It is true that other cases might have come in this category, had the patients lived. For instance, in case six of our series, it was necessary a few days after the pericardiotomy to insert a finger into the wound. Some pocketed pus and a few loose adhesions were detected, and the adhesions were broken up. A year afterward the patient was well and

did not show any evidence clinically of impaired action of the heart. It is too soon to predict the ultimate outcome, but from present appearances the child is completely cured.

Pool had a similar experience, but his patient died thirteen days after the pericardiotomy. In our case, seven firm, dense adhesions were found sealing the heart to the pericardium anteriorly at operation. This patient is now convalescent, but at present it is impossible to foretell whether the adhesions will or will not reform. Savoy, Delorme, Sievers, Stoker and Allingham found an extensive adhesive pericarditis in their cases at autopsy, but none of these patients had survived operation as long as a month.

Drainage—Table 5 gives an idea of the material used and the method of carrying on drainage. Somewhat more than half the opera-

TABLE 5—*Drainage*

	Recovered	Died	Outcome Unknown	Total
Tubes	34	26	0	60
Tubes, but discontinued because of irritating heart	0	1	0	1
Tube, but 1 year later adhesive pericarditis	1	0	0	1
Dakin tubes	2	1	0	3
Gutta percha, then tube	0	1	0	1
Gauze, then tube	0	1	0	1
Rubber tissue or gutta percha	1	2	0	3
Glove drains	1	0	0	1
Cigaret drains	1	0	0	1
Drain protected by condom	1	0	0	1
Gauze then gauze in tube	1	0	0	1
Plain or iodoform gauze	8	5	0	13
Wound left open	4	2	0	6
Pericardium stitched to wound and gauze wick placed in sac	1	0	0	1
Pericardium stitched to wound and gauze wick placed in sac, later tube substituted	1	0	0	1
Not described	14	17	1	32
Not described, died 1 year later of adhesive pericarditis	1	0	0	1
Total	71	56	1	128

tors showed a preference for tube drainage. Usually two tubes were employed, one placed in the culdesac on either side of the heart. Next in popularity came either raw or protected gauze drains. In six cases the wound was left open, and no artificial drainage was used. In another the edges of the pericardium were stitched to the wound, with a gauze wick placed in the sac first but later replaced by a tube. In still another the wound was left open, the pericardium was stitched to the muscles and a piece of gauze introduced a short distance into the sac. In those cases in which the pericardium was stitched to the muscle or skin, a slightly longer time elapsed before the complete closure of the wound occurred, on the whole, there is not much choice between the methods enumerated, all being attended with about the same percentage of primary recoveries.

Lindner, Lane and Lilienthal had to discontinue tube drainage because it impinged on the heart and by irritating it caused a stormy and irregular action. Riedel and Eichel, in pericardiotomies performed for other purposes than a pyopericardium, noticed the same phenomenon

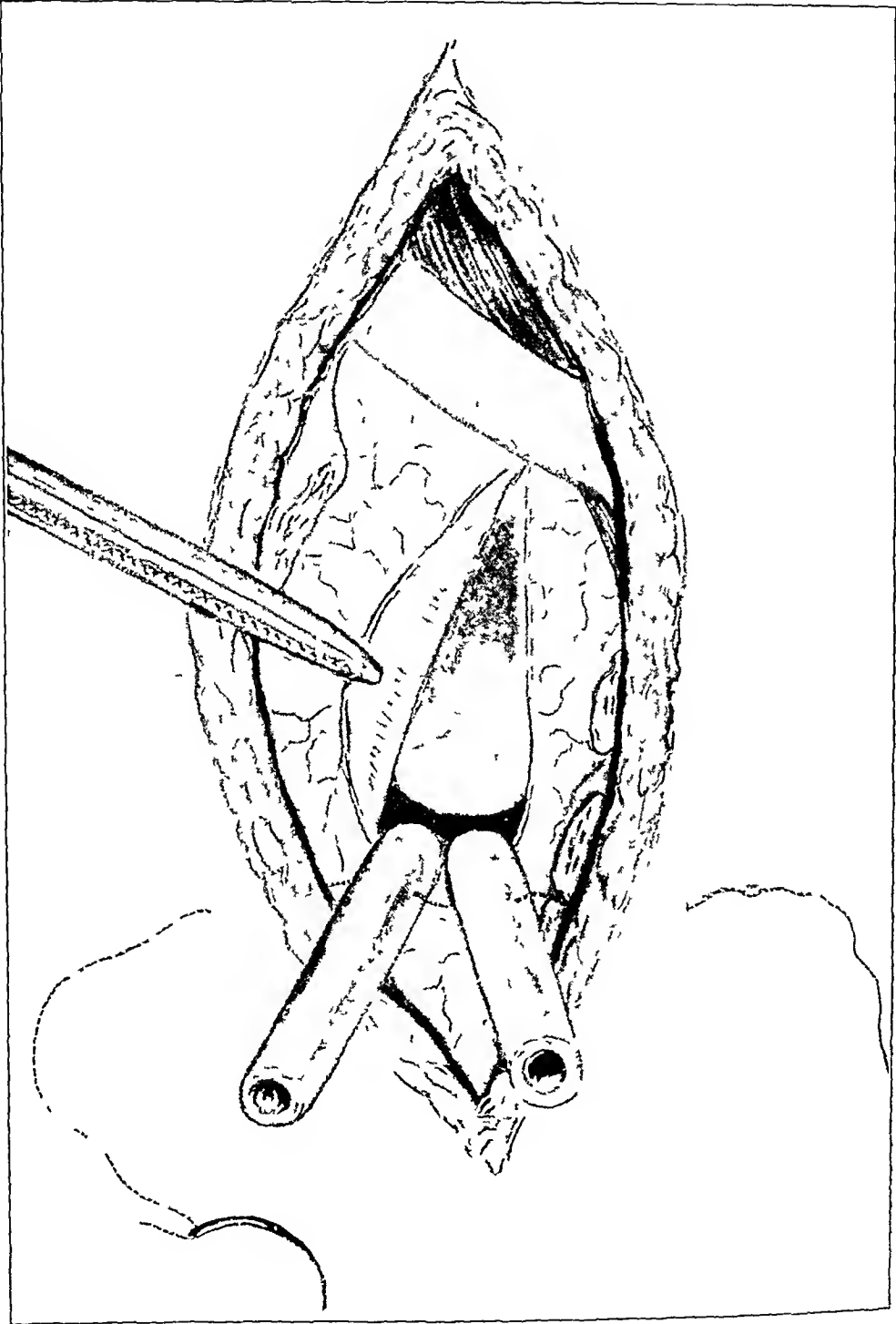


Fig 5—Tubes sutured in position in the xiphocostal approach for pericardiotomy

In Underhill's case, a sharp hemorrhage occurred from the drainage tube two days after the pericardiotomy. This was repeated at intervals until the death of the patient.

Irrigation—Irrigation was used in forty-five of the cases, twenty-four patients recovered and twenty-one died. The solutions used were 3 per cent salicylic acid solution, 1 per cent phenol solution, thymol solution, Condy's fluid, boric acid solution, tincture of iodine, 1 to 10, 0.5 per cent lysol solution, iodoform in glycerine, normal solution of physiologic sodium chloride, bicarbonate of soda solution, sterile water, eusol, - mercuric chloride solution in a dilution of 1:5,000, gentian violet and surgical solution of chlorinated soda.

In sixty-three instances the question of irrigation is not mentioned. Of these patients thirty-nine recovered, twenty-three died, and in one case the outcome is not given. In one of the recoveries adhesive pericarditis had occurred, and death was predicted, in another of the recoveries death occurred later from adherent pericarditis. It is specifically mentioned in twenty cases that irrigation was not employed. Eight patients recovered and twelve died.

Parker's experience illustrates aptly the importance of making provision for the return flow of the irrigating fluid. After the pericardiotomy in his case, the pus did not flow well. It was thick and contained membranous shreds. Irrigation was practiced, but the opening in the pericardium became plugged with lymph, and the pressure of the trapped fluid on the heart proved fatal. Rhodes had a similar experience. While he was washing out the pericardium, the catheter became plugged, the patient grew cyanotic, gave a few convulsive jerks and was apparently dead. The catheter was pulled out; this was followed by a gush of irrigating fluid. Respirations began immediately, and in a few minutes the patient was apparently as well as previously, but he died several days later. Pool, Wood and Bradley, and Stone used surgical solution of chlorinated soda apparently with satisfaction. Jopson used it with great trepidation, and in fact had to discontinue its use because it was not tolerated.

Prognosis—The prognosis, though always grave, is by no means hopeless. Even in apparently moribund patients, striking cures have occurred. Twenty-five patients of this series were so listed, with fifteen recoveries and ten deaths. Of much significance from a prognostic standpoint is the etiologic element. Those cases caused by the introduction of pyogenic organisms directly from without, as from a nonsterile instrument, in which the disease was therefore limited to the pericardial sac, give the best percentage of recovery. The pneumococcic variety

2 Preparation of eusol was described in "Queries and Minor Notes," J. A. M. A. 74:413 (Feb. 7) 1920.

TABLE 6—*Mortality Census*

Case No	Survived Operation	Clinical Impression	Autopsy	Comment
4	30 hours	Pleuritis	Pus in pericardium, fatty degeneration and dilatation of heart, miliary abscesses in lungs and liver	Died in collapse
7	15 days	Pyemia	Abscess in the left thigh, no pus in pericardium, left lung completely collapsed, right serous pleurisy, adhesive pericarditis	During course of disease had normal temperature part of time
8	14 days	Pyemia	Abscess in the left thigh, inflamed left ankle, serous fluid in the left pleura, obliterative pericarditis, mediastinitis	
10	18 hours	Pyemia	Fatty degeneration and dilatation of heart, fibrinous purulent exudate in pericardium, right hydrothorax, obliterative left pleuritis, edema of lungs, purulent bronchitis, thrombosis of pelvic veins, necrosis of kidneys	
11	18 days	Typhoid, congested lungs	Terminal pneumonia, right empyema, left pleural effusion	
12	6 days	Osteomyelitis, pyemia	Left empyema, granulation tissue on inner surface of pericardium, death attributed to pyemia and hemorrhage from pericardium	Two days after pericardiotomy, hemorrhage from drainage tube, ceased spontaneously and recurred with greater or less severity for 6 days, when patient died of exhaustion
14	Died on table	Osteomyelitis	Nothing of importance	Died during operation from trapping of irrigating fluid
15	13 days	Influenza, arthritis	Small amount of pus and large amount of fibrinous exudate in pericardium	Death attributed to myocarditis
16	17 days	Osteomyelitis	No autopsy	Death attributed to pyemia
17	few minutes	Influenza, empyema	Heart adherent to whole anterior surface of pericardium, sero-purulent fluid in lower and back part of pericardium	Death attributed to asphyxia
19	26 days	Influenza, pneumonia, empyema	No autopsy	
21	7 days	Osteomyelitis, pneumonia, pyemia	Bilateral empyema, no pericardial adhesions	Death attributed to syncope and pyemia
23	25 days	Pneumonia	Thrombosis left innominate and jugular veins, myocarditis, pyo-pericardium	
24	12 days	Osteomyelitis	Numerous abscesses in wall left ventricle communicating with pericardial sac, miliary abscesses of kidneys, caseous focus in lung, evidence of pleurisy	Death attributed to heart failure and pyemia
25	6 days	Influenza	Pericardium empty, pus in right ankle and right sternoclavicular joints	Death attributed to sepsis
26	8 days	Pneumonia empyema	Pus in pericardium, bilateral empyema, adhesive pericarditis, acute nephritis	Died in collapse, in the meantime had had thoracotomy for empyema of left lung
27		Primary	Yes	In light of autopsy, disease believed to have originated in anterior mediastinum
33	17 days	Pneumonia	Left pleurisy, infarcted lung, murky fluid in pericardium	In meantime thoracotomy for empyema

TABLE 6—*Mortality Census—Continued*

Case No.	Survived Operation	Chief Impression	Autopsy	Comment
36	30 days	Pneumonia	Pericardial adhesions, some pus in pericardium atelectatic right lung serum in left pleural cavity nutmeg liver, infarcts in both kidneys	Death attributed to heart failure
42	17 days	Pneumonia	Pus in pericardial sac bilateral empyema	Thoracotomy for bilateral empyema performed in the meantime died in collapse
43		Osteomyelitis	Multiple abscesses in the muscle of the heart	Death attributed to pneumonia
45	50 days	Empyema		Death attributed to exhaustion had had empyema 1 year before
46	12 days	Pneumonia empyema	Yes	
47	3 days	Bronchio pneumonia	No autopsy	Death attributed to collapse
48	11 hours	Empyema	Pericardium and both lungs firmly adherent to the wall of the chest, heart adherent to pericardial sac, disease appeared to have originated from a collection of inspissated pus lying between sac and left lung	Death attributed to weakness
50	Few days	Pneumonia		
54	10 days	Pneumonia	No pus in pericardium on the left side pneumonia fibrosis of the right lung	Death attributed to collapse
55	52 hours	Osteomyelitis, suppurative peritonitis		No operation for peritonitis as child's condition did not warrant it
57	Ultimately			Death attributed to general streptococcal infection
59	6 days	Pyemia		Disease followed in miscarriage
60	16 days	Pneumonia	Yes	Death attributed to exhaustion
62	2 days	Tonsillitis pneumonia, empyema	Number of small abscesses in heart with some bleeding both into pleural and pericardial cavities	Pyopericardium discovered and drained through empyema cavity
64	1 month	Pneumonia, empyema, measles	Gelatinous deposit in anterior mediastinum abscess between the heart and left pleura	In the meantime had had right thoracotomy for empyema died of inanition
66	1 week	Pneumonia	Pyopericarditis right empyema suppurative peritonitis	
69	2 days	Measles pneumonia	Gelatinous pus covering both layers of pericardium diphtheritic laryngitis	Diphtheria had not manifested itself during life
70	Later	Osteomyelitis		Death attributed to secondary osteomyelitic processes
73	Eventually	Whooping cough	Abscess at the base of the right lung empyema of the left lung, pus in the pericardium	
81	13 days	Pneumonia		During convalescence had thoracotomy for empyema of right lung
82		Pneumonia		During convalescence thoracotomy for empyema

3 Pyopericardium is not necessarily a lethal condition but its cure depends on pericardiotomy with provision for adequate drainage

4 Operative treatment should yield about 70 per cent of cures

5 The importance of recognizing an associated empyema, whether primary or secondary, cannot be unduly emphasized, for in the event of such a complication, it is only by incision and drainage of the purulent foci in both the pleura and the pericardium that the recovery of the patient may be hoped for

6 Postoperative adhesive pericarditis is not so common a complication as is generally supposed

7 In those patients who recover, longevity is not appreciably compromised

8 A lessening in the mortality rate apparently depends on earlier diagnosis and earlier operation

9 The relatively few instances of pericardiotomy for pyopericarditis do not by any means represent the total number of these patients operated on, for many remain unreported, nor are they a true index of the incidence of this lesion, as by far the larger proportion never reaches the hands of the surgeon

10 The results of pericardiotomy for pyopericardium are necessarily modified by the gravity of the primary disease

11 In a limited number of cases operation has proved unsuccessful because a coexisting or complicating purulent focus has been overlooked, this oversight is especially likely to occur in the presence of empyema, unless great care is exercised

12 Autopsy reports show clearly that suppurative pericarditis is much too frequently overlooked by the internist

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VARICOSE VEINS

ETIOLOGY AND TREATMENT, A CLINICAL AND HISTOLOGIC STUDY *

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DETROIT

The occurrence of varicose veins in the legs in varying degrees of severity, is much more general and frequent than is usually assumed. Relief is sought only in the more advanced cases, usually those in which considerable incapacitation has occurred. While the patient with a more advanced case may bring his malady to the attention of his physician, the less marked and early case is only observed on careful physical examination, and even then only by the physician who notes the condition of the legs with the patient standing. Yet, it is the early case that offers the most favorable ultimate prognosis. Because of the neglect to note this condition, the case records of even the best conducted clinics are not available in determining the frequency. Even a random estimation would not be of value. General observation leads one to feel that varicose veins are of greater frequency among the laboring population, however, when one considers that the majority of the population belongs to this class, the idea loses its significance, other than to impress the fact that the person least able to bear the inconvenience, even unto incapacitation, is the one on whom the burden is wont to fall.

This latter fact, along with the variation of opinion regarding the underlying cause for varicose veins, has been a constant stimulus to me in carrying out those investigations in which I have been interesting myself for some time. Though the problem must continue to be rather vital, I am at present able to throw some light on certain aspects of it. Many of the difficulties are only too obvious. Perhaps insufficient and inaccurate data have caused the most disagreement among those few who have found some degree of interest in the matter. Strikingly little has been done toward getting at the underlying cause of the disease, and much that has been written is open to considerable criticism. Perhaps, also, the fact that animal experimentation presents difficulties that, at present, seem insurmountable has been an important factor in discouraging serious effort toward investigating the disease, a further hindrance lies in the inherent anatomic difficulty, and, finally, a disease that seldom causes death is slow to arouse the interest of the patient himself, or that of the medical profession, regardless of the degree of incapacitation and suffering it may cause. The great majority are inclined to accept such a disease as an unavoidable evil and one that should be

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silently tolerated. Consequently, the meager effort directed toward investigating the cause for varicose veins is traceable both to the inherent difficulties of the problem itself, and to the general attitude of the physician and the patient.

The chief purpose of this paper is to present a study of a series of clinical cases and the results of further histologic investigation regarding the structure of the varicose vein itself. In working with the patients I have been extremely interested in the family history relative to varicose veins. The matter of age at which the disease first appears, the sex, the habits, the condition of the cardiovascular system, as a whole, and the distribution and the character of the veins about the legs, as well as other points in the history and the physical examination, have been carefully considered. Some of the results are doubtless of some etiologic and diagnostic value. In addition to reporting the results of my own work, those of other investigators are briefly discussed, and, since the matter of treatment is of considerable moment, it too, is considered.

CLINICAL INVESTIGATION

This study includes 112 cases, of which seventy (62.5 per cent) were in males and forty-two (37.5 per cent) in females. They were unselected in every respect except one: care was taken not to include any case with a definite history of deep circulatory obstruction, and even some with a negative history in this regard were excluded from the series, because they bore many of the signs of an old deep circulatory obstruction. This was done because it is felt that varicose veins resulting from this cause are of entirely different nature. The distribution of the veins and the appearance of the legs are usually different from what is found in the ordinary type of varices, which I have chosen to call "idiopathic." Those resulting from deeper obstruction have their origin on an anatomic basis, which is easily explained and is sufficient in itself, and further, the treatment in these cases must be along entirely different lines from that usually accepted as good treatment for the idiopathic type.

The histories and examinations were all personally conducted, thus eliminating certain elements of individual variation. They were recorded on the history and examination form as indicated. Some of the points relative to which the patients were questioned are doubtless not important and, consequently, do not deserve comment. All patients were examined in the standing posture, the entire extent of both legs being inspected carefully as regards distribution, size, tortuosity and sacculatation of the veins. The condition of the great saphenous vein above the level of the knee and the presence or absence of edema, pigmentation and ulceration about the lower leg were also noted. The presence or absence of small superficial bluish veins about the feet and ankles seems

to have considerable significance. They are usually noted only in the advanced case of idiopathic varicose veins, or in those cases in which the varicose veins (frequently small and relatively few in number) are due to some underlying circulatory disturbance other than that produced by the varices themselves. These small superficial veins are conspicuous

HISTORY AND EXAMINATION FORM

Name Salmon, Willis S. Case No 72342 Service Surg. Date 1/26/1926

Age 34 Sex M Color W Height 69 Inches

Family History Other causes of varicose veins in the same family Wt 180
2 Bio

- (1) Relationship Paternal grandmother Sex F Age of development — Femoral Thrombosis (yes)
Number of pregnancies before appearance of varices — After 9 (total)
Occupation Housework Hours on feet long Alcohol 0
- (2) Relationship Maternal grandmother Sex F Age of development — Femoral Thrombosis (yes)
Number of pregnancies before appearance of varices — After 6 (total)
Occupation Housework Hours on feet long Alcohol 0
- (3) Relationship Mother Sex F Age of development 30 Femoral Thrombosis (yes)
Number of pregnancies before appearance of varices 3 After 0
Occupation Housework Hours on feet long Alcohol 0

Personal History

Diseases Rheumatism 0 Tonsillitis + Typhoid 0 Gonorrhea 0 Syphilis 0
(Palpitation 0)
Heart trouble (Shortness of breath 0)
(Precordial pain 0)

Habits and Occupation

Hours on feet not long Exposures to extremes in weather (moderate)
(none)
Occupation Telephone engineer for 10 yrs (at desk)
Alcohol 0 Coffee 0 Tea 0 Tobacco 0

Present Illness

Age of appearance of Varices 18 First appeared on left leg at (lower calf)
right leg at (upper calf)
(thigh)
Number of pregnancies before appearance of varices — After —
(none) (yes)
Symptoms (burning) Ulceration (for 12 years) Fem Throm (no)
(pain and fatigue) (none)

Physical Examination

Description of Varices Few small varices over medio-ventral
(with patient standing) aspect of left calf, also, small varix
on dorsum above popliteal area. Occasional small
varix on medio-ventral aspect right calf — Slight
oedema
Location of Ulcers Over tibia at junction of lower and middle third
Saphenous above knees (1) palpable entire (2) visible entire
Hemorrhoids 0 Varicocele 0
Veins on back of pendant hand (markedly, moderately, not) dilated

Heart Nothing abnormal found
Blood pressure Systolic, 170, diastolic, 80
Wassermann (pos, neg)
Other unusual and pathologic findings Constipation

about the ankles of persons suffering from deep femoral thrombosis. What is true of this type of small dilated vein is also true of edema. Little or no edema is seen about the ankles of patients who have idiopathic varicose veins, unless the process is marked and extensive and even then the edema is not of the severe degree often seen in association with deep femoral thrombosis.

Since a rational treatment for the relief of symptoms from varicose veins largely depends on the ability of the surgeon to distinguish the idiopathic type from that produced by various other circulatory disturbances, the general appearance and distribution of the varices were carefully studied and noted in each case. The terms here applied in defining the degree of involvement and areas of distribution are open to considerable criticism, for, at best, they must be quite general. Nevertheless, since all were made by one person, they are open to less criticism than if they had been made by different examiners. In table 1, the number of cases in each group is fairly close, yet the group designated as "moderate involvement" is greatest of the three. Those cases in which the varices were extensive, tortuous and sacculated to varying degrees are placed under the first heading. Those in which the involve-

TABLE 1—*Severity of Varicose Veins*

	No of Cases	Percentage
Marked involvement	30	26
Moderate involvement	50	44
Slight involvement	32	28

TABLE 2—*Condition of Great Saphenous Vein Above the Level of the Knee*

	Male		Female	
	No of Cases	Percentage	No of Cases	Percentage
Involvement	57	50	13	11
No involvement	13	11	20	25
Right leg alone	10	9	6	5
Left leg alone	14	11	5	5
Both legs	33	30	2	2

ment was defined as "moderate" contained many fairly large, tortuous varices without evidence of sacculatation. In each of these groups the great saphenous vein above the level of the knee was usually involved to a greater or less extent. Those cases classed as "slight involvement" had only a few varicose veins, which were only slightly tortuous. The patients were, as a rule, symptom-free, and the condition was noted only on routine physical examination, though occasionally a young woman sought treatment largely for cosmetic reasons. In all cases of idiopathic varicose veins, the distribution about the lower leg appears to be of considerable importance, being almost invariably over the medial aspect of the calf, in other words, it corresponds with the distribution of the tributaries of the great saphenous vein. Involvement of the lateral aspect of the lower leg unless the case is very advanced should always arouse suspicion regarding the underlying cause for the varices (figs 1 and 2). Deep femoral thrombosis injury syphilis diabetes and endarteritis must be carefully ruled out, as, in consequence of the attendant circulatory changes, disastrous operative results may follow the removal of the varices.

From the etiologic standpoint the family history is of extreme interest (table 3). Of the 112 patients, sixty-two (55 per cent) gave a positive family history, and fifty (45 per cent) could not give a definite history, or gave a negative one. These facts seem significant, when one considers that in many instances, the patients could not be expected to

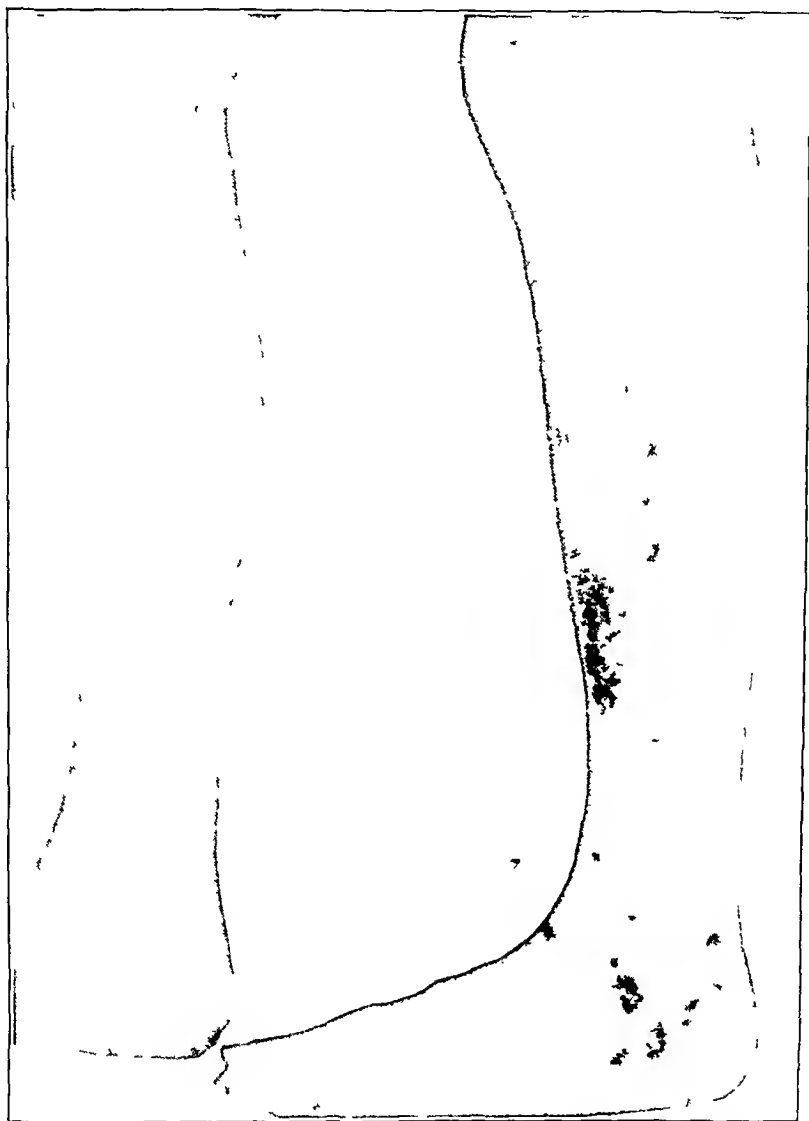


Fig 1—Patient with a history of deep femoral thrombosis of left leg as a complication of influenza pneumonia, nine years previously. Small patch of varices on outer aspect of leg, also pigmentation and scarring extending to below the external malleolus should be noted.

know a great deal about the condition of the legs of other members of their family, especially, might this be true of cases in which the varices may have been slight and were not causing symptoms. With due allowance for this, placing the percentage of patients with a positive family

history at seventy-five doubtless would not be excessive I am confident that heredity is an important factor in the majority of cases This is further borne out in studying the relationship of pregnancy to varicose veins Varicose veins in women who have borne children are generally considered to be due to pressure of the gravid uterus on the iliac vessels,



Fig 2—Same patient as shown in figure 1, absence of varices along medial surface of leg should be noted, pigmentation and scarring from old ulceration are evident below internal malleolus

which thus causes sufficient venous obstruction to bring about the dilatation of the veins of the legs In a previous paper,¹ this was given as one of the more likely causes for varices, however, the results of the present

¹ Nicholson Berlin B Histopathology and Etiology of Varicose Veins, Arch Surg 7 47 (July) 1923

investigation lead me to feel that pregnancy usually plays only a secondary part in the development

Of the forty-two women in this series of cases, thirty-nine were questioned regarding the relationship between pregnancy and the occurrence of the varices. Nineteen (48.7 per cent) had been pregnant before the varices were noted, while twenty (51.3 per cent) had not previously been pregnant.

The age at which the varices were first noticed is of considerable interest and may be of some diagnostic value. The age in each of the 102 cases is recorded in table 4, while in table 5 it is given according to

TABLE 3—*Relationship of Patient to Other Members of Family Having Varices*

Relationship	No of Cases	Relationship	No of Cases
Father	11	Sister	19
Mother	37	Aunt	3
Grandfather	0	Uncle	1
Grandmother	4	Nephew	1
Brother	7	Cousin	1

TABLE 4—*Age at Which Varices First Appeared*

Age	Male	Female	Age	Male	Female
Childhood	2		27	2	2
8		1	28	2	3
13	1		29		3
15	2		30	3	3
16	2		33	1	
17		1	34	1	
18	9	2	35	1	2
19	1	1	36	2	1
20	6	3	38	1	
21		1	39	1	
22	3		40	5	
23	5	1	41	1	
24	1	4	45	2	
25	8	6	50	1	
26	2	2	54		1
Total				65	37

groups. In the latter it may be noted that the ages of preponderance are 18 (eleven cases), 20 (nine cases) and 25 (fourteen cases). Of the 102 cases, seventy-three (69 per cent) were males and thirty-one (43 per cent) females. The latter percentages are significantly close. The occurrence of varices in males during the fourth decade of life is fairly common, however, beyond this period, idiopathic varices rarely, if ever, occur. In the patients here reported whose age was above 40, there is considerable question regarding the deeper circulation. Therefore, the results are in accord with the generally accepted view that varices always develop during early life.

The leg first involved and the relative severity of the process in each leg when both legs are involved are not without interest. It may be noted table 6, that in eighty cases (71 per cent) both legs were involved. Of the remaining thirty-two cases, thirteen (12 per cent)

only the right leg was involved, while in nineteen (17 per cent) only the left leg was involved. It might further be noted that, of the eighty patients with bilateral involvement, fifty-two (65 per cent) were male, while twenty-eight (35 per cent) were female. The greater number being males attracts considerable interest, and several factors may account for this difference. The inference might be that varices are more common in males than in females; this, however, is contrary to the usual view. Further study of the table reveals that the number of cases having the earlier involvement in the right leg equals that having it in the left leg and that about 60 per cent are males. While all these figures are interesting, they probably have little diagnostic or etiologic value.

TABLE 5—*Age-Groups of the 102 Cases in Which the Age of Appearance of Varices Could Be Ascertained*

	Male	Female
Early childhood	2	1
10 to 15	4	
15 to 20	18	7
20 to 25	17	12
25 to 30	9	13
30 to 40	11	3
40 to 50	4	
— to 54		1

TABLE 6—*Distribution of Varices with Reference to Leg Involved*

	Male		Female		Total	
	No of Cases	Percent age	No of Cases	Percent age	No of Cases	Percent age
Patients with both legs involved	52	46	28	25	80	71
Patients with only right leg involved	8	7	5	5	13	12
Patients with only left leg involved	10	10	9	8	19	17
Right leg involved the earlier	32	30	21	20	53	50
Left leg involved the earlier	32	30	19	20	52	50

The observations relative to the cardiorespiratory system are indicated in tables 7 and 8. Forty-two cases (37 per cent) gave at least one of the three symptoms indicated in the chart while sixty-nine (62 per cent) were free from symptoms. It may be noted in table 8, that, of the 112 patients ninety (80 per cent) were found to be free from symptoms while twenty-two (20 per cent) revealed the symptoms noted in the table. In this latter group of cases, only about half of the patients had one or more of the symptoms noted in table 7.

The value of the data recorded in both tables is questionable. The symptoms and signs noted are suggestive of cardiorespiratory trouble, but few cases gave frank signs of cardiac disease. Since the conditions noted may have been observed by men not particularly qualified in cardiology it is doubtful whether the condition of the heart has any appreciable significance. It is however conceivable that should there

be a poor heart action, attended with low pulse pressure and retardation of venous return to the heart, the impairment of the general circulation might have considerable bearing on the etiology of varicose veins. In a certain number of cases, in which there is definite damage to the peripheral vascular area, the relationship is unmistakable, being observed in cases of endarteritis, diabetes and syphilis.

The blood pressure in all cases was recorded. An attempt is made to arrange the readings into groups by multiples of ten. The actual reading was recorded in the chart of each case, but in arranging them as indicated in table 9, each pressure was recorded in the group which it approached most closely. If the blood pressure has any significance at all, it suggests that it is normal for the age of the group, into which the

TABLE 7—*Observations Relative to Cardiorespiratory Symptoms in 111 Patients*

	No. of Cases	Percentage
Patients with symptoms	42	37
Patients without symptoms	69	62
Patients with shortness of breath	32	76
Patients with palpitation	27	61
Patients with precordial pain	15	36

TABLE 8—*Observations Relative to the Heart*

	Male		Female	
	No. of Cases	Percentage	No. of Cases	Percentage
Negative observations	59	65	31	35
Enlargement	6	27	1	4
Systolic murmur	7	32	10	45
Diastolic murmur			1	4
Extra systole	2	9		
Positive cardiorespiratory history	6	27	6	27
Negative cardiorespiratory history	6	27	4	18

greater majority of the cases fall. The few high pressures were in older patients with varying degrees of cardiovascular damage. Of the 112 cases, sixty-eight (60.8 per cent) had a systolic pressure between 120 and 140 mm. and eighty-seven (78.1 per cent) had a diastolic pressure between 80 and 90 mm.

The height of the patients in inches is indicated in table 10, the majority having a stature ranging between 5 feet 3 inches and 5 feet 9 inches, with a general average of 5 feet 6½ inches.

The data recorded in table 11 may or may not have significance. It might be of interest to compare these results with those of a similar number of unselected cases. This, however, has not yet been done. The most striking fact is that nearly all patients have some degree of dilatation of the veins of the forearm, yet likely this may be true for all people. But, if it is not true, it may be surmised that the dilatation represents an inherent tendency toward varicose veins, or that there is poor filling of the right atrium attended with a certain retardation and

congestion of the venous circulation These possibilities should be given further consideration

The symptoms noted and the frequency of their occurrence are indicated in table 12 By comparing this with table 1, it will be noted that 58 per cent of patients having symptoms compares fairly closely with the 70 per cent of patients designated as having marked, or moderate, varicose involvement This bears out closely the impression obtained during

TABLE 9—*Blood Pressure*

Systolic	Male		Female	
	No of Cases	Percentage	No of Cases	Percentage
100	4	3.5	1	0.9
110	7	6.2	6	5.3
120	13	11.6	8	7.1
130	19	17.0	5	4.4
140	15	13.4	8	7.1
150	5	4.4	5	4.4
160	1	0.9	2	1.8
180	5	4.4	5	4.4
200			3	2.6
Diastolic				
50	1	0.9	1	0.9
60	3	2.6	2	1.8
70	15	13.4	6	5.3
80	27	24.1	11	9.6
90	20	18.0	8	7.1
100	2	1.8	10	9.0
110	3	2.6	1	0.9
120			1	0.9
130			1	0.9

TABLE 10—*Stature of Patients*

Height in inches	60	61	62	63	64	65	66	67	68	69	70	71	72	73	74
Number of cases	1	6	4	10	18	9	12	12	9	12	7	6	2	2	2

TABLE 11—*Dilatation of the Veins of the Forearm in 99 Cases*

	Male		Female	
	No of Cases	Percentage	No of Cases	Percentage
Marked dilatation	8	8	1	1
Moderate dilatation	46	46	21	21
No dilatation	7	7	16	16

the course of examining the patients It was the rarest occurrence to find early cases with symptoms The most common symptoms were fatigue and burning each occurring alone or in association with one of the conditions designated in the table

Table 13 gives the observations relative to three conditions frequently associated with varicose veins The total number of patients questioned relative to these conditions were hemorrhoids, 105, varicocele sixty and constipation ninety-four Only 25 per cent of the patients had hemorrhoids of which 15 per cent were males Half of the patients questioned regarding constipation were found to be sufferers

to varying degrees. Of the forty-eight patients, twenty-four were males and twenty-four females. These figures are interesting in themselves, but whether or not they have any bearing on the investigation is problematic. The stasis and the resultant toxic absorption attendant with constipation may have a direct systemic effect, which possibly results in a cardiovascular asthenia and relaxation sufficient to contribute to the process of venous dilatation, ultimately ending in varicose veins. However, since constipation is so common to people in general, it is difficult to carry these considerations to a point beyond the hypothetical.

Of the sixty patients examined for varicocele, twenty-four (40 per cent) were found to have the condition in varying degrees. This is a

TABLE 12—*Most Common Symptoms*

	No. of Cases	Percentage
Patients without symptoms	47	42
Patients with symptoms	65	58
Fatigue	25	28
Burning	29	25
Cramps	8	7
Itching	5	4
Aching	11	9

TABLE 13—*Conditions Occurring in Certain Cases*

	Male		Female	
	No. of Cases	Percentage	No. of Cases	Percentage
Hemorrhoids	16	15	11	10
No hemorrhoids	47	45	31	30
Varicocele	24	40		
No varicocele	36	60		
Constipation	24	25	24	25
No constipation	32	23	14	15

somewhat high percentage, yet it is doubtful that it carries with it any great significance, other than to suggest that the varicose process may be fairly general for the particular individual.

HISTOLOGIC AND ANATOMIC INVESTIGATION

Elsewhere¹ are reported the results of a study chiefly confined to the finer and gross anatomy of the varicose vein itself. This was based on eight sections taken from four patients, and eighteen gross specimens obtained from cadavers. The microscopic sections were studied carefully for evidence of changes in the smooth muscle, connective tissue and vasa vasorum, the gross specimens, with reference to number and position of valves in the great saphenous, external iliac and upper femoral veins, also, the frequency of anastomoses between the saphenous and the deeper veins.

Since the literature is at variance as regards the microscopic anatomy of the varicose vein the level in the saphenous vein from which

the microscopic sections were obtained was carefully noted, for it was felt that much confusion in the picture is due to selection of the tissues at random. This tended to eliminate some of the difficulty in arriving at anything like a definite conclusion, yet, since for each level, the changes noted in a single section might vary from those suggesting the earliest to the latest, the conception of a characteristic picture for each level remained difficult. In fact, the variations in structure noted in each section were so extreme that it was virtually impossible to give a definite description for each level. In almost the same field one might see evidence of hypertrophy and hyperplasia of the muscle cells, along with varying degrees of change in the collagenous and elastic fibers. In the same sections might be seen a greatly thickened area adjacent to one thinned out to a mere membrane (figs 3 and 4). This variation is due to the irregularity with which the vein has dilated. The thin areas represent the walls of sacculations, and, it is at these points, in advanced

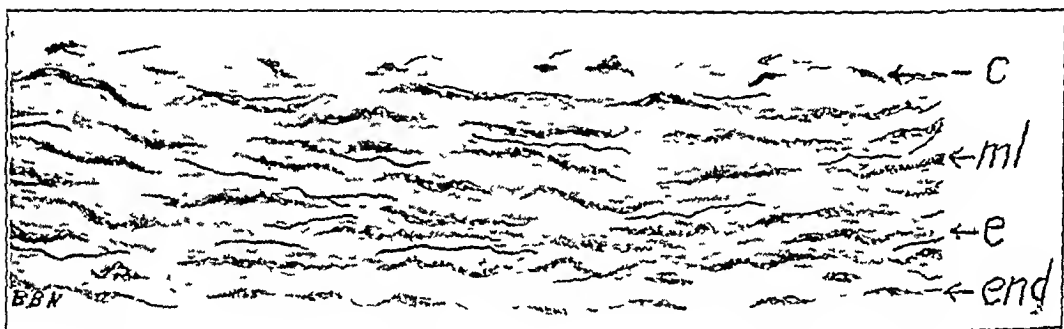


Fig 3—Transverse section of membranous portion of varix above level of knee, *ml* indicates wavy, unhealthy and attenuated, smooth muscle cells containing densely staining, elongated nuclei of irregular outline, *c*, connective tissue cell, *e*, elastic fiber, *end*, endothelium, $\times 400$

varicose disease, that the vein may rupture upon the slightest provocation. Besides this variation in the picture for each level there is a still greater variation for different levels, the more marked degenerative changes being noted below the knee where the hemostatic pressure is greater.

The intima of the great saphenous vein near its opening into the femoral is thickened in areas and contains a considerable amount of smooth muscle longitudinally disposed. In this layer, one may clearly distinguish the nuclei of muscle cells in all stages of amitotic division. This was invariably noted in the thickened areas, in which the muscle cells were much more numerous than in the normal ones. The media at this level is by far the thickest coat and is composed of circularly disposed muscle embedded in connective tissue. There is a distinct internal elastic membrane and a less marked external elastic network. Both of these are composed of coarse elastic fibers, arranged more or less longi-

tudinally The adventitia here is somewhat less thick than the media and is composed largely of connective tissue in which there are many elastic fibers At intervals, longitudinally disposed smooth muscle may be seen The striking feature at this level is the relatively healthy appearance of the tissue and the lack of thin areas in the venous wall

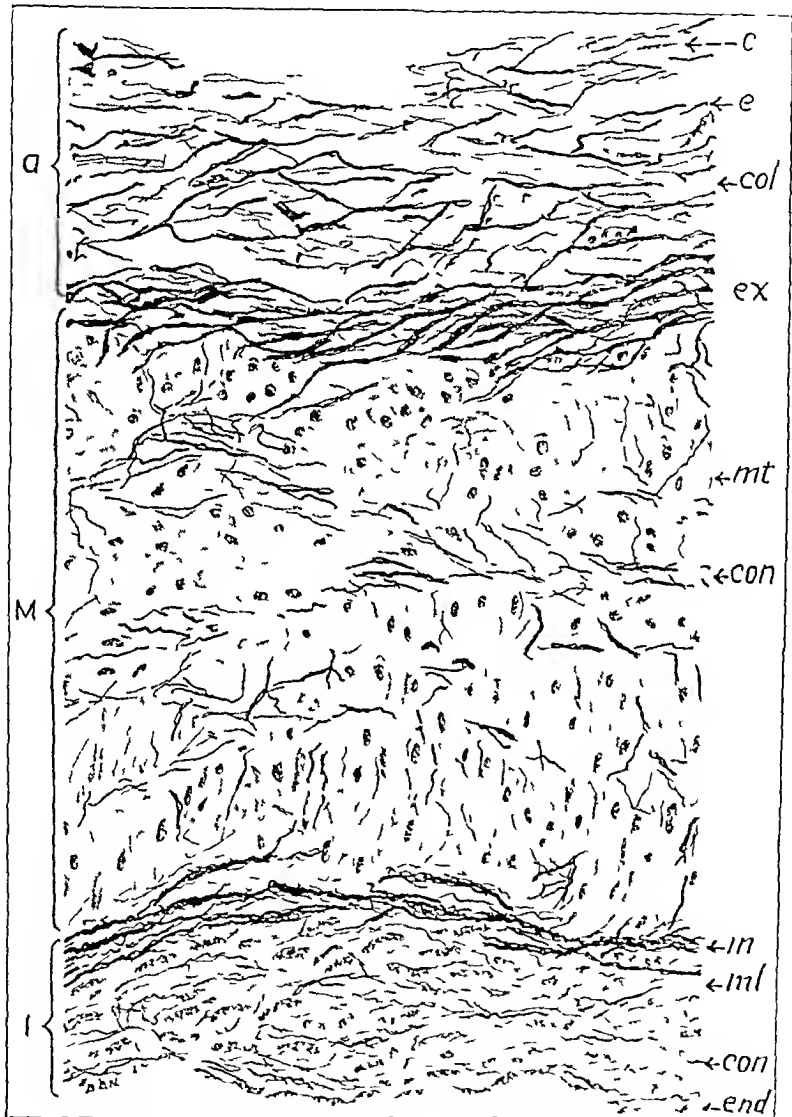


Fig 4—Segment of transverse section of varicose saphenous vein above internal malleolus, *A* indicates adventitia, *M* media *I* intima, thickening internal to internal elastic membrane is evident *con* indicates connective tissue, *col*, collagenous fiber bundle, *c* connective tissue cell *e* elastic fiber, *ex*, external elastic network, *end* endothelium *in* internal elastic membrane *ml* muscle in longitudinal section, *mt* muscle in transverse section $\times 266$

More distal to the saphenous opening there is a less healthy appearance to the muscle, a greater amount of connective tissue a less marked and a less complete internal elastic membrane and perhaps a more gen-

eral thickening of the intima, which may be either internal or external to the internal elastic membrane. Near the middle of the calf of the leg the longitudinal muscle in the adventitia may or may not be found, and at a level above the internal malleolus it is never found. The most striking feature noted in sections taken from immediately above the internal malleolus is the reversal in the disposition of the tissue layers found in the media. Instead of the muscle being circularly arranged it takes a longitudinal course. Likewise, the elastic fibers in the elastic layers and the collagenous fibers in the adventitia are, for the most part, circularly arranged. It might also be further noted that muscle cannot be found in the intima at this distant level in the leg.

The study of the eighteen gross specimens revealed that, in each case, save one, a pair of valves occurred in the external iliac vein, about 3 cm. above the saphenous opening. Six veins had a second pair of valves, from 7 to 10 cm. above the saphenous opening. In every specimen there was a pair of valves guarding the saphenous opening and about 25 cm. below the opening, a second pair could be constantly found. Below these, there was not any regularity of arrangement. The most significant fact, however, regarding the valves in the saphenous vein, below its opening into the femoral vein, was the regularity with which they guarded the orifice of the branches opening into the saphenous vein. Almost without exception, there was a pair of valves just within the mouth of the entering branch, and in those few instances in which this was not true, a pair of valves was found in the saphenous vein immediately below the orifice of the entering branch, which amounts to having them in the mouth of the vein itself.

Various authors have suggested that in certain cases of varicose veins there might be a trophic process involved in bringing about the diseased condition. So, for some time, I have been interested in studying the nerve distribution of the normal and the varicose vein. In this investigation the varicose veins from four operative cases were utilized. Sections from various levels in the leg were chosen. These were treated by the gold chloride technic after the method described by Jordan.² Several variations in the application of the technic were carried out with varying degrees of success. Best results were obtained when small pieces of freshly removed tissue were used and treated for twenty minutes in freshly filtered lemon juice. These were hurriedly washed in distilled water and placed in the dark for one hour in a freshly prepared 1 per cent gold chloride solution. They were again hurriedly washed in distilled water and placed in the dark for forty-eight hours in a 25 per cent aqueous solution of formic acid. After this they were washed, dehydrated, embedded in paraffin and sectioned. Some of the

² Jordan, Harvey E. *A Text-Book of Histology*, New York, D. Appleton & Co.

sections were counterstained lightly with hematoxylin and eosin, but this was of little or no value, for the morphology of the tissue is not sufficiently preserved by the method to be brought out, as it is after being treated in the ordinary fixing agents

The normal veins studied were taken from two recently amputated legs. One was the left leg of a man, aged 34, amputated because of a severe crushing injury to the upper thigh, the other was the right leg of a girl, aged 16, amputated because of a sarcoma of the lower thigh. Both gave histories and evidence of a normal venous circulation. The tissues were removed within an hour after amputation and treated after the technic noted previously.

The tissues from two of the varicose vein cases were so poorly stained that the nerve terminals were inadequately defined. All of the others were sufficiently satisfactory to be used in this study. In some

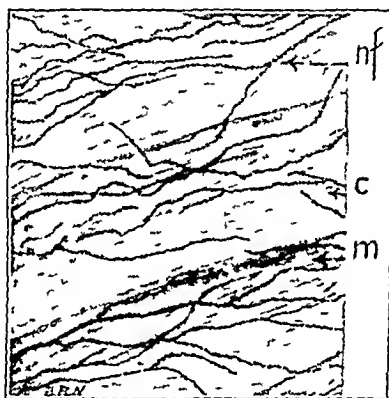


Fig 5—Section of media of saphenous vein, showing *nf*, nerve fibrils, terminating in association with smooth muscle, *m*, *c* intervening connective tissue, $\times 1,000$, gold chloride technic

of them the nerve fibrils were beautifully shown (fig 5). They appeared as delicate, dark slightly tortuous and branching fibers distributed to the muscle bundles. Their appearance was not unlike those described by Laisell³ in the wall of bronchial blood vessels. The knot-like dilatation described by him along the fibrils were not clearly defined. Though there was more or less irregularity in the fibrils this was in all probability due to irregular deposition of the gold salt. The character and distribution of the fibrils did not seem to vary there apparently being as many to the muscle of the varicose vein as to that of the normal vein. In addition to the terminal fibrils themselves many small nerve branches were seen all through the adventitia and outer portion of the media (fig 6).

3 Laisell, O. Nerve Terminations in the Lung of the Rabbit. I. Comp. Neurol. **33** 105 (June) 1921

During the course of these studies part of the tissue was fixed in formaldehyde and stained with hematoxylin and eosin. In studying these, the most outstanding feature noted was the unhealthy appearance of the muscle in the media of the varicose vein, as compared with that found in the same layer of normal veins. In the pathologic material, the cells were somewhat attenuated and the nuclei elongated, pyknotic and more deeply staining than those found in the normal tissue. The characteristic light staining area surrounding the nuclei of normal smooth muscle cells was virtually absent about the nuclei of those found in the varicose vein (fig 7). These results further support the idea

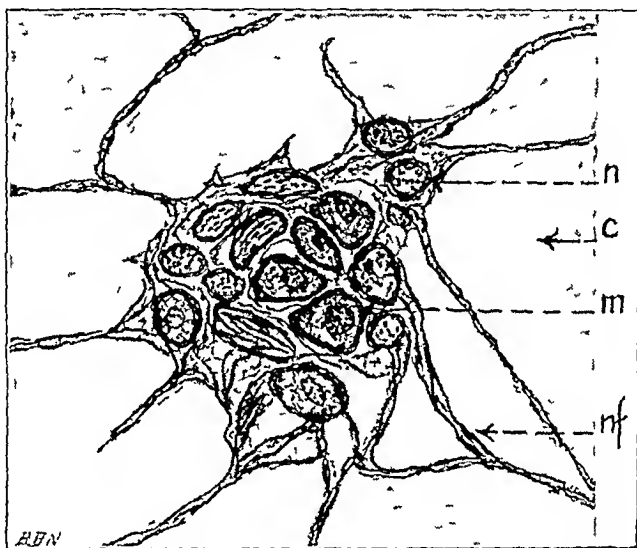


Fig 6—Small nerve trunk found in adventitia of normal saphenous vein, *n* indicates non-medullated fiber, *m*, medullated fiber, *nf*, nerve fibril, *c*, connective tissue, $\times 1,000$, gold chloride technic

that the underlying process in the formation of varicose veins is degenerative, though the factor bringing it about may vary under different circumstances

TREATMENT

The treatment for varicose veins may be directed along three different courses depending on the extent of involvement and the underlying cause. It may be prophylactic, supportive or surgical or even a combination of the three. Regardless of the procedure followed, the result in many cases is far from gratifying and in some it may be disappointing. When the disease is early and the involvement of the veins slight, treatment should be directed toward preventing further damage. This is best accomplished by having the patient work at an occupation which will keep him off his feet at least part of the time. Many think that standing for long hours without being able to walk about promotes the

establishment of varices. Though this contention is not supported by statistics, there may be some basis for it. Considering the physiologic and anatomic factors relating to the circulation of the legs it is easy to understand that the massaging and pumping action of muscles brought into play during locomotion, might improve the circulation sufficiently to keep the musculature of the venous wall in such a state of nutrition and tone, as to prevent the veins from becoming dilated.

Some hold that the anatomic relationship between the vein and the fascia surrounding it, as the former turns inward to enter the femoral vein, is in many cases largely responsible. This, too, lacks conclusive

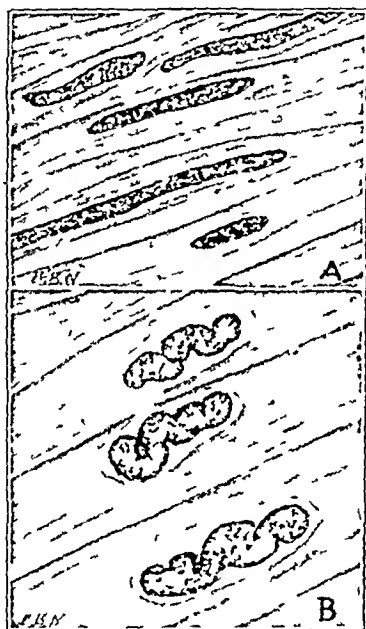


Fig 7—Comparative drawings of muscle found in media of varicose (A) and normal (B) saphenous vein, in A the nuclei are elongated and pyknotic, whereas in B a more normal appearance is observed, the muscle cells being larger and the nuclei being surrounded by the characteristic clear zone $\times 1,000$ hematoxylin and eosin technic

proof but deserves careful consideration and further study. Turner⁴ who is strongly inclined to this view gives a clear description of the anatomic structures involved.

The hiatus in the fascial sheath of the thigh is bounded on the outer side by the iliac portion of the fascia lata which has a sharp well-defined edge known as the falciform border. The upper portion of this known as the superior cornu turns inward superficially to the femoral sheath to join Poirson's Ligament. The lower portion known as the inferior cornu curves inward deep to the termination of the internal saphenous vein but superficial to

⁴ Turner P. Etiology and Treatment of Varicose Veins. Guy's Hosp Rep 73 225-232 (April) 1923

the femoral sheath, to become continuous with the pubic portion of the fascia lata which covers the pectineus and adductor longus muscles and is attached to the ilio-pectineal line of the pubis. Though there is no sharp alteration in direction, the internal saphenous vein here crosses the well-defined inferior cornu of the falciform edge and joins the femoral vein on a deeper plane, the sharp fascial margin intervening between the two vessels. This arrangement by no means necessarily causes obstruction, but it is a relationship where some additional factor may easily produce a slight but definite degree of obstruction which, acting continuously or intermittently over a long period, may produce far-reaching results. The additional factor is, I suggest, increase in the tension of fascia lata. In the sitting or recumbent position the fascia lata is relaxed.

This same author suggests that the relationship between the saphenous vein and the opening of the superficial epigastric, the superficial circumflex iliac and the external pudic vein may, in certain cases, be a contributing factor toward the development of varicose veins. Since the direction of the flow of blood in these veins is downward, and more or less in direct opposition to the current in the saphenous vein, it may be responsible for certain retarding effects on the saphenous circulation. But, if this were true, one might expect to see the first effects in the upper saphenous vein near the point at which these branches enter. Yet it is only a matter of common observation that the upper portion of the saphenous vein rarely becomes varicosed until relatively late in the course of the disease. While the relationship between the upper end of the saphenous and the fascia, and that between the vein and the entering branches, are worthy of consideration, both lack anatomic and physiologic support.

In the early case, accordingly, treatment should be directed toward preventing further increase in the varicose process. Aside from favoring the legs posturally, too strenuous exercise should be forbidden, for a few patients give histories suggesting a definite relationship between vigorous athletics and the occurrence of the varices. In the moderately advanced case there may be some question regarding the preferable treatment. In the majority, external elastic support should first be tried. While it cannot be expected to eliminate the varices it may give considerable relief from symptoms, if there are any, and also prevent the veins from further dilatation. The great difficulty with its application is in getting the patient to carry out the measure faithfully. The wide knit bandage reapplied each morning is the most effective. They are least costly and easily kept clean, though more or less bothersome to apply and to women they are unsightly. Elastic stockings are more readily applied and do not appear so conspicuous through silk stockings, but at best are unsatisfactory. Often they do not fit properly from the first, and usually can be worn only a short time without becoming, to a greater or less degree, ineffective. Furthermore, during the hot summer months patients often complain considerably of the added heat and frequently of excoriation which also adds to the discomfort.

The more advanced case of varicose veins and certain of the less advanced ones are most satisfactorily treated with surgery. Though surgical treatment is at best often disappointing it is thus far the most satisfactory method known for those cases in which the veins are tortuous, thin-walled and sacculated, with probably an overlying pigmented, unhealthy skin. In a number of such cases there may be such a poor state of nutrition of the tissues as to have caused ulceration. The symptoms too may be distressing and, therefore may constitute a further cause for demanding the more radical treatment. As a matter of fact, when the disease seems to be progressive surgical treatment is sometimes justifiable for the purpose of preventing these late and advanced trophic changes, which are not readily relieved after they have once become established. Prior to attempting surgery, an effort should be made to cure any ulceration that may be present. When this is impossible, the sore should be made as free from infection as possible and at operation sealed off from the operative field. The average ulcer responds readily to the treatment usually advocated, but it is of paramount importance to keep the patient off his feet even to the extent of his remaining absolutely in bed.

Before attempting to remove the varices, one should make a careful study of each case to determine the extent of the deep collateral circulation. If this is not done, grief is certain eventually to befall the surgeon. Of prime importance is a careful history to rule out deep femoral thrombosis which may have resulted in obstruction to the deeper venous circulation. Varices coming on after an injury to the leg or pelvis, or even after an illness though definite history of deep femoral thrombosis cannot be ascertained must be looked on with great suspicion. It is not uncommon during the convalescence of a patient to have a slow, progressive obstruction of the deeper veins without the classic symptoms and signs of deep femoral thrombosis ever occurring. The absence of symptoms from deep femoral thrombosis is frequently impressed on us when a sudden fatality from pulmonary embolism occurs following an otherwise simple operation. Frequently the only suggestion of impaired circulation is manifested in the form of undue and prolonged asthenia of the legs possibly attended with slightly painful sensations.

Furthermore, certain of the systemic diseases must be ruled out. Not infrequently as a complication of syphilis, diabetes and certain cases of endarteritis changes take place in the circulatory function of the legs which produce a condition that may easily lead one astray. Attending these circulatory changes varices almost invariably make their appearance, but they usually are not extensive occur relatively later in life than do idiopathic varices and have a more or less characteristic distribution over the leg. The veins involved may be located anywhere

over the lower leg, which frequently is brawny, indurated, edematous and pigmented, and may bear one or more indolent ulcers. Careful questioning will often bring out the fact that the varices appear relatively late with reference to the disease process involving the leg. Even the ulceration itself may appear before, or about the same time, the varices occur. The great saphenous vein above the knee is rarely dilated to the extent of being even palpable. I feel that in many, if not all, of these cases the underlying factor is impaired nutrition of the legs, resulting from some degree of circulatory failure, perhaps most often an endarteritis. The varices represent only another manifestation of failing circulation, rather than being responsible for the failure. The mechanism is probably simple in these cases, as the nutrition of the vessel musculature fails, it fatigues more easily, and, being unable to bear up under the increasing strain, it gradually dilates. This influence, of course, is at work in all types of varices, for, as the varices develop and the circulation becomes less effectual, a vicious cycle is sooner or later established. In the counteraction of this influence lies the only rationale for the use of elastic bandages, stockings and the like.

The treatment in those cases in which the varices depend on some obstruction or impairment of the deeper circulation must be more or less palliative. Any systemic disease must be treated, and if there are ulcers, they must be treated in the usual manner with local applications and by keeping the patient off his feet as far as possible. Even when all of the measures at one's disposal are carried out, the ulcer often cannot be healed. Such ulcers, too, respond poorly to operation. Surgery should be undertaken advisedly and the patient should be fully informed beforehand as regards the likelihood of failure. In some cases the ulceration may be so extensive and the symptoms so severe as to justify amputation. I think, however, that this is not often necessary, though I have seen it so in one instance.

Elastic bandages and stockings in these cases are not well tolerated and lend themselves poorly to the treatment. Usually the venous bed is so poor that any constriction of it increases the symptoms to such a degree that the support cannot be tolerated. As a test for determining the patency of the deeper venous circulation in such cases, the application of a bandage to the lower leg has been advocated. It is doubtful, however, whether this measure is applicable as a differential test in distinguishing between idiopathic varices and those of other origin, yet the test may be of value in determining the volume of the venous circulatory system, regardless of whether it is deep or superficial, or both. Beyond this application, after a consideration of the mechanical and physical factors involved in the procedure the bandaging is of doubtful value. The test is applied by bandaging the leg snugly from the foot to the knee and then allowing the patient to walk continuously for

thirty minutes, or until definite painful symptoms develop. In some cases in which the venous circulation is relatively poor, the bandage is tolerated only a short while. If the evidence points to a scant venous circulation, regardless of cause, operation is contraindicated.

The nature of the surgical treatment of those patients who seem to be fit subjects for operation deserves serious consideration. At the outset, it should be understood that removal of the veins is in many cases unsatisfactory to a greater or less degree. The very nature of the procedure itself makes this true. Because of this, various attempts have been made to avoid some of the difficulties. These have been largely in the direction of varying the method and procedure by which the veins are removed, or their lumen obliterated. Regardless of the method selected, it is more time-consuming than it is difficult.

The usual and most accepted method is excision. However, before any operative procedure is attempted the patient should be examined while standing and the varices should be marked with silver nitrate, or one of the aniline dyes that will not be effaced by the regular surgical preparation of the leg. In the usual case, it is preferable to excise a considerable portion of the saphenous vein above the knee. If this is not done, the varices are likely to recur. One may accomplish the removal by making an incision over the entire length of the leg, but better by making small incisions at intervals along the course of the vein, incising it, passing a probe up its lumen, securing the vein to the probe at the point of the adjacent incision and stripping out the vein through traction on the probe. This lessens the extent of scarring and facilitates healing. The varices of the lower leg are probably best removed through longitudinal incisions made over the most prominent masses. If the incisions are made in this manner the distribution of the cutaneous nerves is not interfered with to any appreciable extent. The classic Schade operation, in which the entire circumference of the leg is incised, no longer commends itself. Even the modified Schade operation in which the incision extends only part way around the leg is probably less satisfactory than that in which the incisions are made in a longitudinal direction over the masses of varices. If an open ulcer is present its excision or incision may promote its healing.

In treating patients with varicose ulcers, Smits⁵ advocates nerve stretching or teasing. He applied his technic to the internal saphenous, the external popliteal, the external saphenous and sometimes the sciatic nerve. He seems to think that the stretching improves not only the ulcer but also the trophic condition of the vessel wall. If the ulcer is large he either cures it or does an excision followed with a skin graft. He reports eighteen cases claiming a cure in all. But

5 Smits J. C. J. C. Varicose Ulcers. *Ann. Surg.* 63: 561 (May) 1916.

since some form of operation for the ulcer was done and, in some cases, even the varices were removed or the saphenous vein was ligated, all of which procedures are the usual ones and carry with them a convalescent period in bed, there remains considerable room for doubt regarding the real value of the nerve stretching operation. To give it credit for the healing of the ulcer seems unfair, when rest in bed alone will bring about healing in the majority of ordinary varicose ulcers.

With the idea of eliminating scar-formation, so far as possible, Keller⁶ has described a method of obliterating the lumen of the varix with a continuous silk suture applied subcutaneously. He first strips out the less tortuous portions of the saphenous through small incisions made along the course of the vessel. The more tortuous portions, which are not amenable to this method, are ligated in segments of from 4 to 5 inches (10.1 to 12.7 cm.) and the lumen of the segment is obliterated by continuous subcutaneous silk sutures which are passed through the vessel wall in such a manner that the latter becomes collapsed, when the sutures are drawn tight and tied. These are left in place for ten days, at the end of which time the lumen has become obliterated through an organized thrombus.

A further method of treating varices without performing an open operation is through injecting the lumen with some substance that produces a thrombus, which subsequently organizes, thus obliterating the lumen. Hitherto, the mere suggestion of such a method would be sufficient to throw discredit on the whole procedure. However, when the shortcomings and disadvantages of the ordinary open operation are considered, any method that is logical and promises something better should not be condemned without careful consideration. The thing most feared in the application of the injection method is dislodgement of a thrombus, with a resultant embolus. Yet, it may be that this danger has been too seriously considered. It should not be forgotten that a fatal embolus not infrequently follows the operative removal of varices. Experimental studies of the injection method will be undertaken in laboratory animals.

This method has been carried out by Douthwaite⁷ in eighty-eight cases, in which over 1,000 injections were made. He has used it for two years, seemingly having complete success, and without recurrences.

"The solution used is composed of quinine hydrochloride 4 Gm., urethane 2 Gm., in distilled water 30 cc. A pneumatic tourniquet is applied with moderate pressure above the line of the vein to be dealt with and 0.5 cc. of solution injected into the lumen through a fine

6 Keller Wm L. Combined Extirpation and Obliteration in the Treatment of Varicose Veins, *Ann Surg* 79 907-912 (June) 1924

7 Douthwaite, A H. The Treatment of Varicose Veins by Injection, *Brit M J* 2 554 (Sept 25) 1926

hypodermic needle. Perivenous administration is usually unnecessary, it is not, however, contra-indicated, as the resultant inflammation is not severe, provided only a few minims are injected outside the vein. The puncture is sealed with collodion, which may be removed the same night, and the injection repeated about two inches further up the vein. It is wiser not to introduce more than 2 cc. at one sitting."

The amount of pain varies considerably, but is usually not severe enough to prevent walking. All patients went to the consulting room "and returned home in their usual manner." "Initial swelling of the vein is not uncommon but this soon subsides and after a few weeks it may be felt as a nodular cord causing no bulging on the surface of the leg, unless it be situated over the subcutaneous surface of the tibia."

Other injecting agents have been used with considerable success, some however, seem to cause severe pain for about one minute after the injection. Dunbar⁸ has treated thirty cases mostly with injections of sodium salicylate. When the salicylate is used care must be taken to test the patient for an idiosyncrasy. Mercury perchloride (1-500) was also used and found to be somewhat less painful.

COMMENT

Though I have only begun to clarify certain aspects of the problem relative to the etiology and treatment of varicose veins I shall feel well repaid for my efforts, should they be of some avail in stimulating others to further researches. As has been suggested, studies in this subject should be as carefully controlled, and as painstakingly worked out as those in any other disease. Yet, this has not been the case. Few have taken the matter seriously. Several have advanced theories regarding the cause while many are indiscriminately removing all varices. The immediate results in many cases are fairly satisfactory while in not a few they are quite the opposite.

The treatment may in all probability remain practically the same yet there is much to be desired as regards the differentiation between the operative and nonoperative case. In the former the results obtained from removing or obliterating the varices may be expected to give the patient considerable comfort while in the latter the results are doomed from the start and the patient to say the least is not benefited and in some instances may even be made worse. In selecting a case for operation one must constantly remind himself of the possibilities for making the patient a hopeless cripple. As most people so affected depend largely on their legs in the performance of their occupation the ultimate result must not be considered lightly.

⁸ Dunbar, J. Treatment of Varicose Veins of the Legs by Injection. Brit. M. J. 1 14 (Jan 3) 1925

Since, also, there is considerable evidence suggesting that heredity and a constant standing posture play an important rôle in the development of varices, much in prophylactic measures might be accomplished. Those who have early varices should be urged to stay off their feet, so far as possible. This is doubly true for those who know of other cases of the disease in their family, regardless of the relationship between its occurrence and any pregnancies that the sufferer may have passed through, for many women have several children without having varicose veins. And, since the majority have the varices occurring before the age of thirty, the condition should be watched for in early youth. Yet, treatment in the early case can seldom be accomplished. In the future, however, much may be done through education.

Though, in the large majority of cases, the hereditary factor seems to play an important rôle, likely other factors are immediately responsible for the primary dilatation. It is not improbable that, in the instance of some veins having a characteristic anatomy various toxic substances and debilitating conditions may be sufficient to initiate the dilatation of the vessel wall. Since the normal function of a vessel is directly dependent on the tone of its musculature, any substance or condition that might produce fatigue might also, after some time, result in dilatation. After the dilatation is once begun various influences tend to promote its increase.

Early in the process, the valves along the course of the vein become incompetent to varying degrees. Nevertheless, contrary to the usual conception of their function they act only in directing the current of venous blood toward the heart and not in the actual lifting of it to that organ. The static pressure in the vein exerted by a column of blood, the upper limit of which extends to the level of the heart, is the same, regardless of the condition of the valves. Granting that the average length of this column is 1 meter and that the average arterial pressure is 110 mm. of mercury, the pressure on the venous wall near the level of the ankle would be 100 Gm. per square centimeter as compared with an arterial pressure of 148.5 Gm. When one considers what ordinarily happens to a vein after the arterial stream is turned into it, the dilatation of the veins of the leg subjected to this pressure, which is equivalent to two thirds that sustained by an artery, should not cause great surprise.

It has been explained elsewhere¹ that, were it not for the siphonic action of the column of blood extending from near the level of the elbow to the opening into the right atrium of the superior vena cava, varices of the hands and arms might be encountered more frequently. As it is, however, the static pressure in the hands, even when in their most dependent position is insignificant.

The motive forces responsible for the venous circulation of the legs are three in number. The most important is the arterial pressure

transmitted through the capillaries into the venules and veins. A slight negative pressure created in the inferior vena cava through the respiratory excursions of the chest wall, and a pumping action resulting from contraction and relaxation of the muscle groups of the legs play some part in lifting the blood through the veins of the leg. The negative respiratory pressure is slight, and can for all practical considerations be neglected. Though the pumping action of the muscles is important it alone could not maintain the circulation. All is dependent on the arterial pressure exerted by the ventricles of the heart. The pumping action of the leg muscles becomes effective only when the blood has been driven into the lower venous branches by the arterial pressure, thus placing it above some of the lower valves. In connection with this action of the muscles, the valves serve one of their most important functions. Owing to their presence the blood is not forced downward. In case of an absence of valves, the muscles would actually hinder circulation rather than aid it. As it is, however, the moment the pressure exerted on the vessel wall by the contracting muscles exceeds that exerted by the arterial pressure, the valves, below the point at which the muscles are acting, close and the muscular pressure forces the blood to a higher level. During the short interval that the valves below the contracting muscles are closed, the weight of the column of blood above is taken off the vessel wall, only during the interval can this be true and even then the vessel wall is not relieved of its load for the transmitted arterial pressure in the vein, distal to the point influenced by muscular force, must be greater than the static pressure normally exerted by the column of blood in the upper portion of the saphenous vein. Therefore it is evident that the valves in the veins can never function in relieving the venous wall of static pressure, for, in order to get the blood into the heart, the transmitted arterial pressure must lift a column of blood extending from a level in the foot to the opening of the inferior vena cava, and, so long as there is any flow toward the heart the valves of necessity must be open along the entire length of the blood stream. When the valve flaps are thrown back they cannot afford any support to the column of blood above.

A further function of the valves is that of directing the blood toward the heart. As brought out previously each branch entering a larger vessel has its orifice guarded by a pair of valves. Were it not for these the blood in the main channels might be forced through the branches and anastomoses thus imposing some degree of delay in reaching the heart. This might especially be true during muscular action when the pressure from the contracting muscles is exerted equally in all directions. If for any reason the valves should become incompetent the blood would be greatly retarded in reaching the heart and would tend to flow back through smaller branches and anastomoses.

Furthermore, the pumping action of the muscles would be lost, or might even become an adjunct to the morbid process. Those branches unprotected by valves would receive much of the blood which, under normal conditions, would be forced to the heart. Under such circumstances, there would be a more or less vicious cycle set up in the veins of the legs, and though, according to Zancani⁹ and others, the prolonged contact of the impure blood with the venous wall might be productive of certain damage, the most deleterious effect, no doubt, is the entailed impairment of nutrition to the tissues. The dilatation and changes found in the vein, therefore, only represent a portion of a nutritional deficiency common to all the tissues of the leg. In the early stages of the disease, this impairment is relatively slight, however, with further dilatation and establishment of incompetence of the valves, the circulation becomes less effective, and, eventually, a more or less vicious cycle is established. When this stage has been reached, little can be expected from a treatment that is not directed at improving the venous return to the heart.

CONCLUSIONS

1 In my series of 112 cases, the number is fairly equally divided between males and females

2 Pregnancy usually is not a cause for varices though in certain persons it may have an important secondary influence

3 Sixty-nine per cent of 102 patients developed varicose veins between the ages of 18 and 30

4 Among 105 patients questioned regarding the leg first involved, the percentage for the right leg virtually equaled that for the left

5 Study of the nerve terminals in the venous wall indicates that varices are not ordinarily trophic in origin

6 The opening of the saphenous vein is always protected by two or more pairs of valves

7 All tributaries entering the saphenous vein are protected with a pair of valves

8 The valves act only in directing the blood stream toward the heart, and not in protecting the venous wall from static pressure

9 In the majority of cases, heredity seems to play an important rôle in the development of varices

10 The later stages and manifestations of varices represent the results of a combination of deleterious influences

11 Treatment may often be difficult and unsatisfactory

12 Great care should be taken in selecting cases for operation

⁹ Zancani, A. Ueber die Varicen der unteren Extremitäten, experimentelle und klinische Untersuchungen, Arch f klin Chir 96 91, 1911

ROENTGEN-RAY TREATMENT OF TUBERCULOUS CERVICAL LYMPH GLANDS

A STUDY OF ONE HUNDRED AND FORTY-ONE PATIENTS TREATED
BY SMALL DOSES OF FILTERED ROENTGEN RAY WITH
FOLLOW-UP RESULTS *

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Roentgen discovered the "X" or unknown rays at Wurzburg in 1895. The active or chemical powers of the rays were first recognized through the destructive burns received by the numerous new experimenters. The burns at once suggested the possibility of a new agent for the destruction of morbid tissues, notably those of the skin including tuberculosis.

In 1902, Dawson Turner,¹ medical head of the electrical department of the Royal Infirmary, Edinburgh, published the third edition of his "Manual of Practical Medical Electricity." On page 376 under the subheading, "Enlarged Tubercular Glands" he writes

"Six cases of enlarged tubercular glands have been under roentgen-ray treatment in the Electrical Department of the Royal Infirmary. The exposures have been of five minutes duration, three times a week. The duration of the disease has varied from thirteen years to three months. In some of the older cases many operations had been performed and sinuses were present. The glands affected were cervical in five cases and axillary in one. In all these cases marked improvement has been brought about, and in two of them a complete cure (duration of these latter, eighteen months and seven months). I am not aware of any other recorded cases of this treatment of this disease and credit of the initiation of this treatment lies with Dr Hope Fowler, the assistant electrician of the Royal Infirmary.

This places the first recorded use of the roentgen ray in glandular tuberculosis about the year 1900.

In 1902, F. H. Williams² of the Boston City Hospital in his book reported that even the largest glands responded surprisingly well to treatment with the roentgen ray.

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* Read before the Saratoga Lake Medical Society, Jan. 9, 1924.

* Owing to lack of space this article is abbreviated by the use of the protocols of 141 cases. The complete article appears in the author's paper.

1. Turner, D. "A Manual of Practical Medical Electricity," 3rd ed., 1902, p. 376. Rays and Fluorescent Light, ed. 3, New York, William Wood & Co., 1902, p. 376, ed. 4, 1904, p. 397.

2. Williams, F. H. "The Roentgen Rays in Medical Work," 1st ed., New York, The Macmillan Company, 1902, p. 674.

In 1903, F P Vale³ reported the case of a patient with the disease who was favorably affected following roentgen-ray treatment. Searching the literature, Vale discovered Turner's as the first record of roentgen-ray treatment of the disease.

In 1903, Pusey and Caldwell⁴ reported five cases in which the patients were treated by them with favorable results.

Since 1903, there has appeared much medical writing on this subject in many languages. Most of this work has been lean in details of technic, meager in the proof of results, and almost lacking in follow-up reports, but there has constantly sounded an unmistakable ring of sincerity in the observations published proclaiming favorable and curative effects of the roentgen ray on tuberculous lymph glands. The mass of empiric evidence affords great support to the use of this therapeutic agent.

In the autumn of 1917, at the Presbyterian Hospital in New York, there was started a special clinical study of patients with tuberculous glands of the neck. This work has been consecutive and is still in progress. While controlled by the department of surgery, including outpatients and inpatients, all departments of the hospital have been available for the work. The report herein presented is that of the first four years during which efforts were mainly directed to the therapeutic use of relatively small doses of filtered roentgen ray, with follow-up results. A few of the observations herein given have appeared in a preliminary discussion of the indications for operation in this disease,⁵ but I beg to submit them again in their full context.

OTHER THERAPEUTIC AGENTS USED BESIDES THE ROENTGEN RAY

It became evident from the first that treatment could not conscientiously be limited to the roentgen ray alone. Therefore, in a majority of the patients some of the following additional measures were used:

Attempts were made to improve the general hygiene.

All foci harboring simple and tuberculous infection, such as tonsils and adenoids, were treated.

Rest was prescribed as needed, sometimes rest in bed.

Cod liver oil and "tonics" were prescribed as appeared helpful.

Surgical dressings were applied to wounds and sinuses.

3 Vale, F P. A Brief Note on the X-ray Treatment of Glandular Tuberculosis, *Wash M Ann* 2 324, 1903.

4 Pusey, W A, and Caldwell, E W. The Practical Application with Roentgen Rays in Therapeutics and Diagnosis, ed 1, Philadelphia, W B Saunders Company, 1903, p 393, ed 2, 1904, p 417.

5 Hanford, J M. The Indications for Operation in the Treatment of Tuberculous Cervical Lymph Glands, A Preliminary Report, *Ann Surg* 80 885 (Dec) 1924.

Minor surgical operations, such as aspiration, incision, curettage and small biopsy, were performed.

Major operations were performed, that is, attempts were made to excise a lesion or a group of lesions.

The patient was treated for tuberculosis elsewhere in the body.

The patient was treated for ailments such as constipation or other nontuberculous disease.

Patients were urged to seek, and sometimes arrangements were made to provide, sunshine, fresh air, good food, better environment and rest. Specialists were employed to examine and to treat the nose, throat, ear, skin, mouth, eye and chest. Small doses of cod liver oil were used over long periods in almost every case.

I made nearly all of the surgical dressings and performed most of the operations. The dressings were simple, consisting largely of the use of minute amounts of 95 per cent phenol for the sinuses and of sterile petrolatum. Skin irritants were avoided during the period of roentgen-ray therapy.

OPERATIONS

It might be argued that the operations alone favorably changed the course of the disease, that they—not the roentgen ray—were the main feature of the treatment, that particularly the major operations in certain cases brought about the result. Sixty-nine of the 141 patients submitted at some time to some form of operation.

Aspiration of one cystic swelling plus twelve roentgen-ray treatments was associated with complete resolution (case 159). My experience has shown that aspiration alone has little or no therapeutic value in cystic or in fluctuating tuberculous lesions in the neck.

The operation of incision with or without curettage of sinuses or abscesses was performed forty-three times. Most of these were simple incisions of which fifteen were performed within a month before the roentgen-ray treatment was started and twenty-eight during treatment or soon after it ended. The fifteen patients on whom incisions were made before treatment had reached at the start of their treatment the sinus stage of the disease. Of the twenty-eight patients on whom incisions were made after treatment had been begun, nineteen appeared to have had the softening induced by the roentgen-ray treatment. There were two in whom the lesions softened under roentgen-ray treatment without incision, so it is interesting to note that twenty-one of the 141 patients appeared to suffer "cold" abscess formation as a result of the roentgen-ray exposures. Incision of cold abscesses is generally regarded to be inadequate treatment.

Five partial excisions included two types of lesions. In the case of one patient there was simply excision of a protruding granulation

over a sinus opening (case 4) In the other four there was incomplete and unsatisfactory removal of sinuses and of the indurated tissue about them (cases 114, 145, 161 and 181) In case 4, the operation was a failure, while two roentgen-ray treatments resulted in quick healing In cases 114, 145 and 181, the operation undoubtedly played a large part in the ultimate good results Other lesions existed in addition to those operated on, and the roentgen ray may have been an important factor in the apparent healing of these remaining lesions

Fifteen radical excisions were made By the term radical excision is meant an attempt to excise completely a lesion or a group of lesions It does not necessarily include all the lesions in the neck For example, in case 42 a mass was excised from one side of the neck before roentgen-ray treatment was started on another lesion on the opposite side In this case the mass treated mainly by the roentgen ray became resolved and apparently remained healed The side on which the operation had been performed was not directly treated with the roentgen ray, and the lesions recurred forty-seven months later There were three other cases in which excisions of main lesions were made, the smaller lesions being treated with the roentgen ray These cases have been classed according to the smaller lesions, which may or may not have been favorably influenced by the excisions Roentgen-ray treatment of these three patients (78, 136, 150) resulted in apparent cure or in marked improvement

Eleven patients on whom radical excisions were made belong to a third class, namely, those in whom results of roentgen-ray treatment over longer or shorter periods were not satisfactory Sometimes the patient or I was dissatisfied too soon perhaps Cases 109, 117, 123, 129, 133, 154, 163, 164, 173 and 176 belong in this group The reports are based on what occurred up to the time of the radical excision, and the roentgen-ray results are given accordingly Biopsy, or the removal for examination of a very small part of the diseased area, may be discounted as a factor in treatment

To summarize, then, the influence which the operative procedures may have had in the results, I may say that only the partial excisions and the thorough curettings appear important These together have influenced the course of the disease in only thirteen of the 141 patients I believe that the surgical procedures have played but a minor part in the results presented

Few physicians would expect definite effects on tuberculous lesions in the neck from the other general therapeutic measures used Seven of the patients received other specific antituberculosis treatment in addition to roentgen-ray therapy In case 10 the patient was given tuberculin at an eye clinic for ocular tuberculosis The ultimate effect

on the neck was slight. In cases 14 and 67, the patients received enough ultraviolet light to produce a good tan, but both required more than three years from the time of this treatment to show their ultimate apparent cure. In cases 47 and 100, the patients received good treatment at a sanatorium over several months. The former was undoubtedly thus helped to his final apparent cure, while in the latter the result was not favorable after treatment at the sanatorium. In cases 51 and 127, the patients had a whole summer's rest in the country. The former said that she thought roentgen-ray treatment brought about her apparent cure, the other showed marked improvement in the neck at the end of her rest, but she had received five roentgen-ray treatments before going to the country.

Thirty-two patients received no other treatment that might have affected the results.

It is fair to state, therefore, in studying the clinical course of the 141 patients, that the roentgen ray was the predominating specific therapeutic agent employed.

ROENTGEN-RAY DOSAGE AND TECHNIC

The roentgen-ray dosage which held good for all but a very few cases was about one third of the dose of filtered roentgen ray necessary to produce a slight erythema in an average person. In a few exceptions curiosity led to a trial of about two thirds of the erythema dose. These exceptions are indicated in the protocols.

The patients received appointment cards with two weeks fixed as the interval between treatments. The number of treatments advised was not fixed at first but was gradually increased up to ten which was finally chosen as the minimum number of treatments for all patients. Such a series lasted about four and one-half months. More treatments were then given to some patients who were not markedly improved by the end of the series. Some who had recurrences later received a second series of treatments. Table I gives the details of the roentgen-ray dosage. The hair and surrounding parts were protected with lead although this precaution probably is not necessary in using small doses once in two weeks. At first only the diseased side of the neck was treated but during most of the time both sides were treated. One third of the erythema dose was used on each side so that the total dosage to the lesion was somewhat increased by this cross firing. One treatment means one session of roentgen-ray exposure whether one or both sides were treated and always includes direct treatment of diseased tissue in the neck. No attempt was made to exclude the thyroid glands. The tonsils and pharynx were also exposed. The parathyroid and pituitary glands were usually thought to receive enough exposure.

The smaller doses of roentgen ray were selected for this work because of the extreme susceptibility⁶ of the lymphoid cell to the roentgen ray, because of the disadvantage of massive destruction of these cells which almost certainly play an active part in resistance to the disease,⁷ because of the probable stimulating effect of small doses on the production of lymphoid cells,⁸ because at the time I began, fewer reports had been published on the results of small doses than of large doses, because they are safer and can be given oftener, thus allowing the physician to observe the patients more closely, because my aim was to induce resolution without softening (softening appeared more likely to occur with the larger doses), and because it was thought the reactions from the larger doses were more likely to interfere with appetite, nutrition and general health

The roentgen ray is essentially more convenient and less expensive than radium, and, for this disease, probably equally good

TABLE 1—*Details of Dosage**

Tube	First Two Years		After First Two Years	
	Coolidge (Broad focus universal type)		Coolidge (Broad focus universal type)	
Anode skin distance	25 cm		25 cm	
Filter	Flint glass	4 mm	Aluminum—3 mm	
	Wood	1 cm		
	Bakelite	4 mm		
	Aluminum	1 mm		
	Leather	6 mm		
Spark gap	8½ inches		8 inches	
Milliamperes	About 5		5	
Number of minutes exposure	4 to 5		4	
Milliampere minutes	21 to 25		20	
Area exposed (approximate)	7 inches in diameter		7 inches in diameter	

* Interval of treatment desired was two weeks to one area. For the two periods the dosage was essentially the same, i. e., about one third of an average erythema dose

6 Taylor, H D, Witherbee, W D, and Murphy, J B. Studies on X-ray Effects I Destructive Action on Blood Cells, *J Exper Med* **29** 53, 1919

7 Murphy, J B, and Ellis, A W M. Experiments on the Role of Lymphoid Tissue in the Resistance to Experimental Tuberculosis in Mice, *J Exper Med* **20** 397, 1914

8 Thomas, M M, Taylor, H D, and Witherbee, W D. Studies on X-ray Effects II Stimulative Action on the Lymphocytes, *J Exper Med* **29** 75, 1919. Nakahara, W. Studies on X-ray Effects III Changes in the Lymphoid Organs after Small Doses of X-rays, *J Exper Med* **29** 83, 1919. Nakahara, W, and Murphy, J B. Studies on X-ray Effects V Effect of Small Doses of X-rays of Low Penetration on the Lymphoid Tissue of Mice, *J Exper Med* **31** 13, 1920. Studies on X-ray Effects VII Effect of Small Doses of X-rays of Low Penetration on the Resistance of Mice to Transplanted Cancer, *J Exper Med* **33** 429, 1921. Murphy, J B, Liu, J H, and Sturm, E. Studies on X-ray Effects IX The Action of Serum from X-rayed Animals on Lymphoid Cells in Vitro, *J Exper Med* **35** 373, 1922. Nakahara, W, and Murphy, J B. Studies on X-ray Effects X The Biological Action of Small Doses of Low Frequency X-rays, *J Exper Med* **35** 475, 1922

CONDITION OF PATIENTS AT BEGINNING OF TREATMENT

General Condition—The group was unselected, except that patients with active pulmonary tuberculosis were usually rejected. These were placed elsewhere for treatment. Tables 2, 3 and 4 give the ages, nationalities and occupations. There were ninety-seven females and forty-four males, a ratio of more than two to one. Sixty-five of the patients had relatively normal general health and sensation except in the neck, but a large number of these had diseased foci of secondary infection, seventy-one, a majority, were below par, being pale, thin, tired, weak, nervous and having headaches or colds. Three had syphilis, one,

TABLE 2—Ages of Patients at Start of Roentgen-Ray Treatment

Ages, Years	No. of Patients	
1 to 10	28, about $\frac{1}{5}$	} About $\frac{5}{6}$ were under 31
11 to 20	36, about $\frac{1}{4}$	
21 to 30	54, about $\frac{1}{3}$	
31 to 40	9	
41 to 50	9	
51 to 60	4	
61 to 70	1	

TABLE 3—Nationalities or Races

	No. of Patients		No. of Patients
American	33, about $\frac{1}{4}$	Finnish	1
Irish	27, about $\frac{1}{5}$	Swedish	1
Italian	18, about $\frac{1}{8}$	French	2
Jewish	11, about $\frac{1}{12}$	Greek	2
Colored	10, about $\frac{1}{14}$	Austrian	1
Bohemian	5	Danish	1
Scotch	5	Chinese	1
Hungarian	4	Polish	1
Norwegian	4	Dutch	1
German	4	English	1
Russian	3		

acromegaly, and one, simple adenomatous goiter. Of the seventy-one whose health was below par, fifty-four presented evidence of healed or active tuberculosis elsewhere than in the neck (table 5). There were thirty-one with healed tuberculosis and twenty-three with active tuberculosis. Twenty-five presented evidence of healed tuberculosis of the lungs. Thirteen patients with active tuberculosis of the lungs were admitted to the group contrary to our general plan. Seven of these had incipient or slight chronic pulmonary disease while six were in febrile state. Some difficulty in the way of better care held this for some time in our group. There were ten patients with active solitary gland tuberculosis. Tuberculosis of the axillary lymph glands was not simply as a chance extension from the neck with or without evidence of the disease in the neck. Exceptions to this category were

The smaller doses of roentgen ray were selected for this work because of the extreme susceptibility⁶ of the lymphoid cell to the roentgen ray, because of the disadvantage of massive destruction of these cells which almost certainly play an active part in resistance to the disease,⁷ because of the probable stimulating effect of small doses on the production of lymphoid cells,⁸ because at the time I began, fewer reports had been published on the results of small doses than of large doses, because they are safer and can be given oftener, thus allowing the physician to observe the patients more closely, because my aim was to induce resolution without softening (softening appeared more likely to occur with the larger doses), and because it was thought the reactions from the larger doses were more likely to interfere with appetite, nutrition and general health

The roentgen ray is essentially more convenient and less expensive than radium, and, for this disease, probably equally good

TABLE 1—*Details of Dosage**

Tube	First Two Years		After First Two Years	
	Coolidge (Broad focus universal type)		Coolidge (Broad focus universal type)	
Anode skin distance	25 cm		25 cm	
Filter	Flint glass	4 mm	Aluminum—3 mm	
	Wood	1 cm		
	Bakelite	4 mm		
	Aluminum	1 mm		
	Leather	6 mm		
Spark gap	8½ inches		8 inches	
Milliamperes	About 5		5	
Number of minutes exposure	4 to 5		4	
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TABLE 3—*Nationalities or Races*

	No. of Patients		No. of Patients
American	33, about $\frac{1}{4}$	Finnish	3
Irish	27, about $\frac{1}{5}$	Swedish	3
Italian	18, about $\frac{1}{8}$	French	2
Jewish	11, about $\frac{1}{12}$	Greek	2
Colored	10, about $\frac{1}{11}$	Austrian	2
Bohemian	5	Danish	1
Scotch	5	Chinese	1
Hungarian	4	Polish	1
Norwegian	4	Dutch	1
German	4	English	1
Russian	3		

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patients as may show definite tuberculosis of an upper limb, of the breast or wall of the chest. When axillary disease coexisted, it was also treated with the roentgen ray.

Not all of the tonsils removed were examined. In three cases, however, they proved to be tuberculous. Relatively few tonsils and adenoids were removed at that time because it was hoped that the roentgen ray would tend to heal them and to decrease their size. I

TABLE 4—*Occupations of Patients*

	No. of Patients		No. of Patients
School	43	Laundry	1
Housework	25	Chemist	1
None	15	Teacher	1
Domestic service	11	Telephone installer	1
Clerical work	9	Actress	1
Textile worker	4	Business man	1
Saleswoman	3	Barber	1
Dressmaker	3	U. S. A. war service	1
Porter	2	Bellman	1
Machinist	2	Insurance agent	1
Chauffeur	2	Shoemaker	1
Nurse	1	Ship waiter	1
Tailor	1	Janitress	1
Printer	1	Violinist	1
Attendant	1	Policeman	1
Artist	1	Pipefitter's helper	1
Telephone operator	1		

TABLE 5—*Patients with Tuberculosis Elsewhere as Well as in the Neck, as Found at the Commencement of Treatment—54**

(A) Healed 31 Patients		(B) Active 23 Patients	
Lungs and thoracic lymph glands	19	Axillary glands with healed tuberculosis of lungs	6
Thoracic lymph glands alone	3	Axillary glands with active tuberculosis of lungs	2
Skin	1	Axillary glands with tuberculosis of upper limb	1
Pleura alone	1	Axillary gland	1
Lower limb	1	Lungs and abdominal lymph glands	1
Upper limb	1	Lungs, tonsils and adenoids, skin (ribs developed during treatment)	1
Frilipian tubes (removed)	1	Lungs (and thoracic glands)	9
Peritoneum		Lower limb	1
Abdominal lymph glands	3	Inguinal glands	1
Axillary glands	1		
Peritoneum			

* Eighty seven, or 61.7 per cent of the whole group of 141 were without evidence of healed or active tuberculosis elsewhere.

now believe that all patients fit for the operation should have their tonsils and adenoids removed, whether or not they show evidence of disease, and that this should be done at the start. This opinion is based on the inability to detect tuberculous tonsils and adenoids which may continue as active foci unless removed, despite the chance of their being cured by roentgen-ray treatment.

A composite picture of the general condition of these 141 patients shows that they were active and ambulatory and generally able to carry on their occupations. I share with others the impression that there is a

mild tuberculous toxemia in all patients with active cervical gland tuberculosis. As a rule they are slightly below normal in health.

Local Conditions of the Neck—As the cervical disease existed in this group, it exhibited a variety of lesions which occurred singly or in complex combinations. To analyze and classify these has been difficult. Dowd's⁹ division into groups I, II and III was first considered, but so many of our cases fell into groups II and III, that is, into the more advanced and atypic forms, that a different arrangement seemed advisable. Accordingly, they have been grouped by the specific type of lesion so that the results in several different types may be studied.

In a recent article,¹⁰ I called attention to a working pathology of the clinical forms of the disease. Briefly it is this: 1 The first lesion is a firm swelling. This may be either large and markedly visible or only moderately large and not prominent. 2 The next phenomenon is a faintly elastic or cystic swelling. Liquefaction necrosis in the first lesion has rendered it cystic. 3 The same process brings the third lesion of definite softening and fluctuation, the "cold abscess." 4 The spontaneous or surgical opening of the cold abscess produces the sinus, the fourth lesion. The four main types of the disease are: firm swelling, cystic swelling, fluctuating soft swelling (that is, "cold abscess") and a sinus that tends to persist. There are two others which are of less importance clinically because their treatment is included, as a rule, with that of the four main lesions. These are first, skin tuberculosis at sinus openings and in the walls of abscesses, and secondly, extreme fibrosis. Ugly scars are frequent sequelae of the disease, and it has been interesting to see the apparently favorable effect of roentgen-ray treatment on them.

The enlarged firm swellings have been divided into two groups, large and small. There is a difference in the actual mass of disease in these two groups, and larger swellings are decidedly more of a therapeutic problem. The large swellings have been designated as those estimated to be more than 2 cm. in diameter and the small swellings as those under 2 cm. Thus there may be a swelling of a single gland or of a group of glands. Many of the patients had more than one type of lesion. I shall discuss the results of treatment both on the patients and on the various lesions studied as pathologic-clinical entities.

There were 115 patients who at the beginning of roentgen-ray treatment had firm swellings, of which sixty-eight were large and forty-seven small. Ten had cystic swellings, nine had cold abscesses,

⁹ Dowd, C. N. Tuberculosis of the Cervical Lymphatics. *J. A. M. A.* 67:499 (Aug. 12) 1916.

¹⁰ Hanford, J. M. Some Applied Pathology of Tuberculous Cervical Lymph Glands, *Internat. Clin.* 4:115 1923.

and fifty-six had sinuses. One hundred patients had but a single type of lesion at the beginning of roentgen-ray treatment. Forty-one had two or more types. This grouping of the single types of lesions does not apply entirely to the cases in which there were enlarged glands, for despite the presence of smaller glands in some of the patients with large glands, these cases were listed only as cases of large glands. Many of the patients in the sinus stage of the disease were so classified because the cold abscesses had been incised within a month before the first roentgen-ray treatment. These could not be said to have had "persistent" sinuses, but it is believed that they were potentially "persistent." A sinus may be called persistent if it does not heal within two months after its appearance. The majority of the abscesses incised just before roentgen-ray treatment actually resulted in such persistent sinuses.

TABLE 6—*The Period Elapsed (as Taken from the Clinical Histories) from the First Appearance of Tuberculosis in the Neck Until the Beginning of Treatment**

6 months or less	38 patients	4 to 5 years	6 patients
6 to 12 months	22 patients	5 to 10 years	21 patients
12 to 18 months	3 patients	10 to 15 years	9 patients
18 to 24 months	10 patients	15 to 20 years	7 patients
2 to 3 years	13 patients	20 to 40 years	2 patients
3 to 4 years	10 patients		
			141 patients

Thus over two thirds of the patients had first had a tuberculosis in the neck more than six months prior to roentgen ray treatment, about three fifths more than twelve months, over one half more than eighteen months.

* These earliest lesions may or may not have healed before patients joined this group. This table is shown simply to indicate the persistence and recurrence evident in this group of patients.

Table 6 shows how long prior to the first roentgen-ray treatment the patients had had tuberculosis in the neck. Many of these earlier lesions had disappeared or healed before the appearance of the new ones which brought the patients under my care.

EVIDENCE OF TUBERCULOSIS

In 56 per cent of the cases the diagnosis was based on microscopic examination of tissue, on inoculation of guinea-pigs or on roentgen-ray evidence of calcification¹¹ corresponding to the lesions in the neck. These cases have been considered as "proved" tuberculous. In the remaining 44 per cent, the diagnosis was based on the clinical picture, including history, physical findings and the course of the disease. These are the cases "accepted" as tuberculous. The evidence for the diagnosis in each case is given in its protocol. Most of them were diagnosed as tuberculous by several clinicians. All doubtful cases have been excluded.

11 Hanford, J. M. The Roentgen Ray Diagnosis of Tuberculous Cervical Lymph Glands. *Am J M Sc* 164: 539 (Oct) 1922.

TREATMENT

The Value of Treatment—It is almost impossible to prove the effect of any particular form of conservative treatment for a disease which tends to heal spontaneously, though slowly, and which usually responds slowly to all conservative treatment. I shall discuss conservative treatment, not radical excision. Conservative treatment as I have indicated in a recent paper,¹⁰ means any method of treatment short of an attempt to excise a lesion or a group of lesions.

Three questions must be considered. 1. Has treatment altered the natural course of events? 2. Does one method of treatment take effect more quickly than others? 3. Does one method of treatment give more permanent results than others?

Since in many cases of various types the disease apparently disappears or there is great improvement for varying periods without treatment, evidence in favor of a method of treatment must include these points:

1. The patient must show definite improvement within a reasonable length of time, in other words, there must be a significant time ratio between the duration of the disease before treatment and the appearance of definite improvement after the beginning of treatment.

2. The longer the follow-up period, the more conclusive is the evidence concerning the durability of the improvement.

3. A given method of treatment must be compared with the natural course of the disease and with other methods of treatment.

The disease does not disappear spontaneously in all cases, sometimes it persists for years. However, significant data on a large untreated group are not available for comparison. Many factors influence resistance and resolution, such as the general condition and age of the patient, pulmonary tuberculosis, the extent of the disease in the neck and the virulence of the infection. These factors vary considerably in different parts of the world.

It may be assumed that New York City has advantages over other localities here and abroad where studies of treatment have been made and reported. In New York the milk supply has been well controlled for many years, free hospitals abound, and people tend to seek medical aid early, pulmonary tuberculosis is on a steady decline, the poor are chiefly immigrants or the children of immigrants, and these people are generally healthier than their relatives in Europe.

Analysis of Observations from Beginning of Treatment—An analysis of the protocols of the 141 patients, including an analysis of the lesions of the neck, has led to the tabulation of some of the results and to a simple statement and discussion of others.

If tables ¹² 7, 8 and 9, are examined, it will be seen that about two thirds of all the patients had had the active disease in the neck for more than six months before roentgen-ray treatment was given, and that about one half of them had had it for more than eighteen months. In table 8 it is seen that more than three fifths of all the patients showed some degree of local improvement within two months after the first roentgen-ray treatment, and about four fifths of them within three months. Table 9 indicates that about two fifths of all the patients showed marked improvement within three months after the first treatment, three fifths within six months, and nearly four fifths, a great majority, within nine months. These facts indicate answers to question 1 and to proposition 1 in the preceding paragraphs. In a majority

TABLE 7—*Duration Before Treatment of the Active Lesions Treated*

2 months or less	25 patients	4 to 5 years	3 patients
2 to 4 months	15 patients	5 to 10 years	13 patients
4 to 6 months*	12 patients	10 to 15 years	4 patients
6 to 12 months	29 patients	15 to 20 years	2 patients
12 to 18 months†	3 patients	20 to 40 years	2 patients
18 to 24 months	10 patients	Record not obtained	2 patients
2 to 3 years	11 patients		
3 to 4 years	10 patients		141 patients

* Eighty nine, a little less than two thirds, had had their active lesions for more than six months before treatment.

† A little less than one half, for more than eighteen months.

TABLE 8—*The Period After the First Roentgen-Ray Treatment Before the Appearance of Any Improvement*

1 month or less	62 patients	Over 4 months	6 patients
1 to 2 months*	29 patients	None	13 patients
2 to 3 months†	15 patients	Doubtful	8 patients
3 to 4 months	8 patients		141 patients

* Ninety one, over three fifths, within two months.

† One hundred and six, nearly four fifths, within three months.

of the cases treatment appears to have altered the natural course of events, and the patients have shown definite marked improvement within a reasonable length of time.

Further, from table 10 it appears that almost one half of the patients were apparently cured in a fair average time of ten months from the first treatment. Only such patients as were apparently cured at their

12 The term "marked improvement" is used to mean so great a decrease in the size of swellings that they become barely visible and possibly healed. Marked improvement usually implies that conservative treatment has been satisfactory to patient and physician alike. In "apparent cure," the contour of the neck has returned to normal, swellings have either gone or become mere kernels, and sinuses have healed securely. I prefer this term to the term "cure." A "fair average" has been reached by eliminating isolated extremes, with the hope of obtaining more reliable generalizations to point the way

latest follow-up visit are included here. This period of time for the attainment of apparent cure is shorter by a month or so than the period indicated by Metcalf¹³ for tuberculin treatment. Metcalf states that "purely glandular cases respond, as a rule, to tuberculin treatment within a year." In his own series, the average duration of treatment of patients who did not have pulmonary involvement was fourteen months and twelve days. Rollier¹⁴ states that "under the influence of heliotherapy the healing of tuberculous glands is almost invariably rapid, three to six months usually being sufficient to cause permanent arrest of the disease in a case uncomplicated by septic infection." Yet no confirmative data are presented except the case of a patient whose lesions did

TABLE 9—*The Period After the First Roentgen-Ray Before the Appearance of Marked Improvement*

3 months or less*	52 patients	Over 12 months	8 patients
3 to 6 months†	33 patients	None	21 patients
6 to 9 months‡	17 patients	Doubtful	4 patients
9 to 12 months	6 patients		—
			141 patients

* About two fifths

† Three fifths within six months

‡ Nearly four fifths within nine months

TABLE 10—*An Indication of the Time Required for the Attainment of Apparent Cure*

	Four Average Time
Small glands	10 months
Large glands	17 months
Cystic swellings	5 months
Sinuses	8 months
	40
	10 months

Sixty seven patients or 47.5 per cent of the group as a whole became apparently cured in a four average time of ten months from the first roentgen ray treatment. Only those are included who appeared cured at their latest follow up visits.

not heal for eleven months after the beginning of heliotherapy at Leysin. I saw another patient who was apparently cured after having been retained at Leysin eleven months for treatment.

One hundred and eleven patients (78.7 per cent) received five or more treatments while thirty received fewer than five. In these thirty the treatment was not effective in 50 per cent as against the group as a whole in which the treatment failed in only 29.1 per cent. Only slight improvement may be expected from fewer than five treatments.

13 Metcalf W. B. Tuberculosis of the Lymphatic System. New York: Macmillan Company, 1919, pp. 249-260.

14 Rollier A. Heliotherapy. London: H. Frowde, 1923, p. 101, d. 2.

The advocates of small doses are beginning to recommend the continuance of treatment even after apparent cure or marked improvement. L. J. Carter¹⁵ recommends twenty-four treatments with relatively small doses. I feel that it is advisable to give more than ten treatments over a period of from six to ten months. It is interesting to note that this is about the period found advisable by the advocates of tuberculin (Metcalf¹³), and of natural heliotherapy with life in the open air (Rollier¹⁴ and LoGrasso¹⁶).

Recurrence in the original or in new lesions of the neck was found in twenty-seven patients who had shown marked improvement or apparent cure following the roentgen-ray treatment. Had these cases not been followed up, they might have been considered uninterrupted "cures." Eleven recurrences were patently due to active foci of secondary infection, either chronic or incidental. Three patients had syphilis and refused antisyphilitic treatment. Their glands, however, were definitely tuberculous. Two had pulmonary tuberculosis. Eleven recurrences were not explained.

The importance of clearing up and of preventing active foci of secondary infection is the main point in the whole question of recurrence. Recurrences may occur after any method of treatment, for living tubercle bacilli may be retained and may become active during an acute respiratory infection. A method of treatment which will insure complete destruction of the bacilli is not known, and these bacilli may cause recurrences decades after their original activity. Small nodes, apparently healed, sometimes enlarge slightly during an acute infection of any kind and then quickly subside. This is probably not a recurrence but a simple infection, and it indicates that neither the disease nor the treatment has blocked the lymphatics connected with these glands. The supposed fibrosis might be expected to do this, and does in some cases. The causal relation of the roentgen ray to fibrosis in this disease is difficult to estimate, because fibrosis without the roentgen ray is often a striking feature of the pathologic change.

Improvement in general health was noticed in fifty-two of the 141 patients during or soon after their period of treatment with the roentgen ray. There was a tendency for fewer infections of the head and throat to occur. This gives rise to the theory that roentgen-ray treatment of an active tuberculous lesion produces an effect like that of tuberculin. If this could be proved, it might have valuable practical application.

15 Carter, L. J. The Treatment of Tuberculous Cervical Adenitis, Results from Use of Fractional X-ray Dosage in 100 Cases, *J. Radiol.* 2:22 (Sept.) 1921.

16 LoGrasso, Horace. Heliotherapy in Tuberculosis, *New York State J. Med.* 22, No. 6 (June) 1922.

Only slight and occasional temporary, harmful constitutional effects resulted from these small doses. A boy, aged 6 (case 93), received fifty-six treatments of the neck in interrupted series over a period of three years. Twelve months after the last treatment, the neck was relatively normal, and he appeared to be unharmed by the treatment. Evidently the skin, thyroid, pituitary and salivary glands were not injured. His complete blood count was normal. Another patient (case 14), a young woman who had received forty-nine treatments, presented the same observations.

A few patients, not more than five or six, experienced immediate or early unpleasant effects from treatments with small doses. Two noticed itching or burning of the feet. Three felt nausea the same or the next day. One appeared greatly disturbed, she had pains, vomited and felt depressed. Decrease in dosage decreased the symptoms in all the patients.

Nine patients presented cold abscesses at the beginning of the roentgen-ray treatment. Some of the abscesses opened spontaneously, some were incised, and some were excised. Resolution did not occur otherwise in any of them. Only two of the abscesses which were incised were curetted, and curettement was incomplete. All the abscesses finally healed, except the one which received only one roentgen-ray treatment.

There was one cystic swelling which became an abscess during treatment and finally resolved without opening or incision (case 56). This was the only instance of such resolution.

I believe that cold abscesses should be excised or incised and curetted before roentgen-ray therapy is given. Aspirations have been tried and abandoned. Cold abscesses as such are not in a condition to receive maximal benefit from roentgen-ray therapy in smaller doses, except as increased softening and liquefaction may ensue therefrom.

Roentgen-ray treatment of new and old scars has appeared to be effective. They are made smoother, softer, paler, more pliable and less conspicuous. During the period of roentgen-ray treatment the skin must be protected from other irritants. Iodine and sunlight are the commonest, but all topical remedies must be free from irritating qualities.¹⁷ One patient, a girl of 17, was urged to take sunbaths (case 176). She did so and included the neck. She then received two treatments over this sunburned skin. When seen within a few months and again three years later, she showed visible telangiectases—like a "birthmark." This is the only instance of local permanent injury attributable to the treatment and it should have been avoided. On the

¹⁷ MacKee, G. M. and Andrews, G. C. Irruptions Caused by the Roentgen Rays or Radium and Topical Remedies. *J. A. M. A.* **77**: 148, 1921.

other hand, a number of the patients were quickly relieved of the slight pain and soreness felt in the neck before treatment

Enlarged glands showing large areas of calcification in a roentgenogram may nearly disappear under roentgen-ray therapy, so that the contour of the neck returns to normal. In other cases, extensive calcification may limit the decrease in swelling.

From these studies I have observed that lesions in the lower part of the neck, mainly in the supraclavicular region, resolve more readily than those above. This may be due partly to their relative immobility, their distance from the common foci of secondary infection and their protection by the clothing. However this may be, I find that it is often difficult to make a radical excision because they adhere to the subclavian and to the lower part of the internal jugular vein and to the thoracic duct.

The follow-up period of from two months to five years after the last treatment (table 11) is too short to warrant final conclusions as to

TABLE 11—*The Follow-Up Period After the Last Roentgen-Ray Treatment*

Number followed, 120, or 85.1 per cent. The fair average follow up period for the group of 141, as a whole, was 13.1 months. Of the 141, sixty one, or 43.9 per cent, were followed for more than one year. A few were followed for four years or more.

19 patients were followed for 6 months or less

39 patients were followed for 6 to 12 months

30 patients were followed for 12 to 24 months

31 patients were followed for over 24 months

1 patient was followed with record of time doubtful

the permanence of the improvement. It is certain, however, that there are unexplained recurrences in the same, or in new areas, even in necks apparently cured, and after many treatments.

While the literature has not revealed statistics on this point, I have concluded that slight improvement and probably marked improvement and apparent cure are noticed sooner after the beginning of roentgen-ray treatment than after any other form of conservative treatment, particularly tuberculin treatment and perhaps heliotherapy.¹⁸ If this is true, it gives roentgen-ray therapy the advantage of earlier encouragement to patient and physician. Another comparative advantage of the roentgen-ray over tuberculin is its apparent safety immediately after operation on tuberculous tissue and also in the presence of fever. The small doses insure slight (if there be any) tuberculinization. After working personally with tuberculin and with roentgen ray, I feel that the roentgen ray is far superior to tuberculin, from every standpoint and that if the roentgen ray is used, tuberculin is not necessary.

If five cases showing unusual irregularity of treatment are eliminated, the average period of roentgen-ray treatment for the 141 patients

18 Heliotherapy at certain geographical points probably is superior

as a group was 6.56 months. Fifty-eight patients actually received consecutive treatment for six months or more, eighty-three for less than six months.

There were six deaths. Three were caused by pulmonary tuberculosis, one by abdominal tuberculosis. These patients were among those difficult to place in sanatoriums at the beginning. A colored child (case 103) died of acute miliary tuberculosis after having developed dactylitis and Pott's disease following a partial excision in the neck, and after roentgen-ray treatment to the neck was begun. This is the only patient of the whole series who may have had serious constitutional effects from the treatment, that is, from overirradiation (') of an active lesion. One patient died of intercurrent disease which did not bear any relation to the tuberculous glands.

Table 12 indicates the incidence of tuberculosis developing elsewhere during or soon after the period of roentgen-ray treatment. I cannot account for the development of the condition in the eyes. The

TABLE 12—*Active Tuberculosis Elsewhere Than in the Neck or Axilla Which Developed During or Soon After the Period of Roentgen-Ray Treatments—7 Patients*

Eye	2 patients
Eye, dactylitis, spine	1 patient, a small colored boy who later died of acute miliary tuberculosis
Ribs, skin, lungs (tonsils and adenoids)	1 patient, a small colored boy
Tonsils and adenoids	3 patients found tuberculous after removal

* The tonsils and adenoids were probably tuberculous before treatment.

two colored boys should have received country air and sun. All tonsils and adenoids removed from patients with enlarged cervical or axillary glands should be examined for tuberculosis.

A study of the literature perhaps not complete has failed to reveal convincing follow-up results on any conservative method of treatment. Large and small doses of roentgen ray, tuberculin heliotherapy, injections and aspirations,¹⁹ Beck's paste, autogenous vaccine plus tuberculin,²⁰ hyperemia and simple hygienic treatment have not been reported on in sufficient detail in regard to follow-up results. Statistically in selected cases radical surgery⁹ appears to give better results than any other single form of treatment. It conforms to the three test questions stated. Attempt at radical surgical removal is applicable only to a certain percentage of cases as even today many patients do not come to our clinics for treatment until they are in the advanced stages of the disease.

¹⁹ Calot, F. *Indispensable Orthopedics*, ed. 2. London: Baillière Tindall & Co., 1921.

²⁰ Bonime, Ellis. *Tuberculin and Vaccine in Tubercular Affections*. The N. Y., The Southworth Company, 1917.

The disease is so frequently self-limited, with varying success, that assumed results following any method of treatment must be analyzed critically. Furthermore, recurrences and recrudescences often appear so late in life and so long after the disease has subsided, that a report on a large series of permanent cures is almost impossible in one generation. If compelled, then, to deal with facts in such a study as this, the number and value of the justifiable conclusions are not such as to make the reader enthusiastic about the benefits of any plan of conservative treatment. A comparison of different plans would be more helpful were it not for variations in the stages of the disease, in age, race and environment, and for the usually unknown incidence of the types of bacillus encountered.

CONCLUSIONS

1 Small doses of filtered roentgen ray given at intervals of less than three weeks appear to shorten the course of the disease and to favor resolution or marked improvement in all stages (except cold abscesses) in a sufficiently large percentage of cases to justify the conclusion that the roentgen ray is useful in the treatment of tuberculous glands of the neck.

The usefulness of roentgen-ray treatment compares favorably with that of other single methods of conservative treatment, but adequate data on all methods, especially follow-up results, are lacking.

2 A definite superiority of small doses of filtered roentgen ray over other single forms of conservative treatment cannot be proved, but is supported by these observations. (Natural heliotherapy at selected sites may be superior but should not exclude roentgen-ray therapy.)

3 This form of roentgen-ray treatment apparently does not cause undesirable effects not easily avoided.

4 Small doses of the roentgen ray are inferior to the radical surgical treatment as reported by Dowd.⁹ However, his patients on whom radical operation was strikingly successful belonged to a selected group composed largely of children, most of whom were operated on in the early stage of the disease. Hence, even radical surgery might give little better results than the roentgen ray in such an unselected group as this, in which most of the patients were older and were in advanced stages of the disease.

5 From a study of the lesions (tables 10 and 13) I found that (a) The best results appeared in the treatment of patients who had tuberculous sinuses, of whom 76.8 per cent apparently were cured. Eight months after the first treatment was the fair average time for the attainment of apparent cure. The sinuses, however, received the largest number of treatments. (b) The small glands (2 cm —) improved more satisfactorily than the large glands (2 cm +). (c) Forty per cent of

the cystic swellings resolved without incision or spontaneous opening. Hence, some cystic swellings resolved and are therefore different from the definite abscesses. (d) The cold abscesses all resulted in sinuses. These abscesses are not suitable for treatment with the small doses of the roentgen ray except as this treatment may increase liquefaction prior to incision.

TABLE 13—Summary of Results

	Types of Lesions						
	The Patients	All Enlarged Glands, Large and Small	Large Glands 2 Cm +	Small Glands 2 Cm -	Cystic Swellings	Cold Abscesses	Sinuses
Number	141	115	68	47	10	9	50
Fair average duration of active lesions before roentgen ray	See table 7	31.8 mos	39.2 mos	24 mos	1.66 mos	2.6 mos	6.8 mos
Fair average number of treatments	9.4	9.8	11.1	8.6	8	11.7	12
Fair average period of treatment	6.56 mos	7.2 mos	8.3 mos	6.1 mos	4.4 mos	10.4 mos	8.8 mos
Fair average interval between treatments*	19.5 days	19.7 days	19.9 days	19.5 days	16 days	21 days	21 days
Fair average time after start of roentgen ray for appearance of slight improvement	See table 8						
For appearance of marked improvement	See table 9						
For marked improvement or apparent cure		9.8 mos	11.5 mos	8.1 mos			
For appearance of apparent cure	See table 10				5.3 mos		8 mos
Fair average, follow up period for one patient	13.1 mos see table 11	12.0 mos	10.7 mos	13.4 mos	15 mos	18 mos	17.9 mos
Slight or no improvement at last follow up visit	41 29.1%	29 25.2%	19 28%	10 21.3%			1 2.2
Marked improvement through last follow up visit	31 22.4%	1 2.6%	21 31%	10 21.3%			
Apparently cured, through last follow up visit	67 47.5% see table 10	52 45.2%	25 37%	27 57.4%			1 2.2
Marked improvement or apparent cure through last follow up visit	100 70.9%	86 74.8%	40 59%	57 78.7%			

* Though the desired interval was two weeks between treatments, various causes led to the actual average interval.

6 From table 13, allowing for fair averages, it is seen that the whole group of 141 patients with all types of lesions in the neck received 9.4 treatments during 6.56 months with an interval of 19.5 days between treatments.

7 Table 10 shows that 47.5 per cent of the whole group apparently were cured in a fair average time of ten months from the last treatment. Only those who were apparently cured at the time of their last follow-up visit are included.

8 In addition to those who apparently were cured, 23.4 per cent of the whole group were so markedly improved when last seen as to make the treatment appear satisfactory.

9 At the end of a fair average follow-up period of 13.1 months (table 11), conservative treatment, with small doses of filtered roentgen ray as the main agent, appeared satisfactory in 70.9 per cent of all the patients.

10 Tuberculosis of the cervical lymph glands is primarily a surgical problem because, even with conservative treatment, surgical judgment, minor operations and careful surgical dressings play an important rôle. Indeed, major operations are frequently indicated.

11 Treatment of the disease should be comprehensive and not limited to any single method.

POSTOPERATIVE HYPOGLYCEMIA

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As the study of postoperative hypoglycemia is still a subject of interest to both surgeon and internist we consider the following study worthy of report. The work is unavoidably incomplete, and there are only a few cases. However, the method of investigation is new, and the results obtained by its use give infinitely greater understanding of the significant changes in carbohydrate metabolism than does the older method of studying only the whole blood sugar. This method is offered to those who care to study the condition further, with the hope that it will be employed, and with the belief that the results will be of greater physiologic significance than those obtained by any other of the present methods. The method was devised by one of us (L F) for the study of insulin reactions¹. It is simple and can be carried out in any laboratory or well equipped office.

The stimulus for this work was found in Holman's preliminary report on hypoglycemia following thyroidectomy for exophthalmic goiter². He showed that the blood sugar might be below the normal limit, usually from twenty-four to thirty-six hours after operation and suggested that this hypoglycemia might be at least partly responsible for the postoperative reactions. This opinion was suggested by the close resemblance of many of the reactions to the well known insulin reaction, and was strengthened by observing the marked clinical improvement in the patient after the intravenous administration of solutions of dextrose. Our results tend to confirm the report of Holman.

The method depends on a study of the distribution of glucose between plasma and erythrocytes in serial samples of oxalated venous blood. In collecting the specimens of blood, care must be observed to prevent accumulation of erythrocytes in the vein by prolonged use of the tourniquet. A sample is taken before operation. After operation samples are taken serially as often as desired—sometimes this extends

¹ From the Departments of Medicine and Surgery of Western Reserve University and Lakeside Hospital.

¹ Foshay, L. Observations Upon the Action of Insulin on the Blood with Special Reference to the Cause of the Condition Known as Hypoglycemia. *Am J Physiol* **73** 470 (July) 1925.

² Holman, E F. Hypoglycemia in Exophthalmic Goitre. A Preliminary Report. *Bull Johns Hopkins Hosp* **34** 69 (Feb) 1923.

over a period of several days. If any unusual symptoms are observed in the patient, a sample is taken immediately.

In our work, determinations of blood sugar were made on the whole blood in the usual manner. Any accurate method may be used. The remaining blood was centrifugalized in a calibrated tube until the cells were packed into a homogeneous mass. We found that 1,500 revolutions a minute for fifteen minutes was sufficient. The volumes of the whole blood and of the cells were then read, and the proportions of plasma and cells calculated. A determination of the sugar was made on plasma and the corpuscular glucose was calculated according to the following formula

$$\text{Cell sugar per cent} = \frac{\text{whole blood sugar per cent} - (\text{plasma sugar per cent by plasma volume per cent})}{\text{cell volume per cent}}$$

Each determination of sugar was made in quadruplicate by the method of Hagedorn and Jensen.

Eight patients were studied, on four, thyroidectomies had been performed for exophthalmic goiter, on two, herniorrhaphies, a large lipoma had been excised from the region of the shoulder on one, and on the other a cholecystectomy had been performed.

The first patient with a goiter who was studied had had a subtotal thyroidectomy performed thirty hours before we saw her. About twenty-four hours after operation, tachycardia, flushed skin and profuse perspiration were observed, and she complained of profound weakness. This reaction was transient and strongly suggested a deficiency of available glucose in the tissues of the body. The first specimen of blood was examined six hours after the reaction and showed a normal content of glucose in both plasma and cells. Eighteen hours later, or forty-eight hours after operation, the patient had a similar but milder reaction. Analysis of the blood showed a normal content of glucose in the whole blood and plasma but a marked reduction of corpuscular sugar. This reaction was also of brief duration, and treatment was not required. No more reactions occurred. Examination of the blood two days later showed a normal distribution of glucose.

The second patient with goiter had determinations of the sugar made before operation and at five different intervals after operation. No reactions were observed, and there were no variations in either the concentration or the distribution of blood glucose. The low reading of the plasma sugar in the specimen of blood taken forty-seven hours after operation was probably an error.

The last two patients with goiter were first seen during similar reactions. In one case, the reaction was mild and associated with a moderately low corpuscular sugar and normal plasma sugar. It disap-

peared promptly after some food was given by mouth. The blood sugar was normal in both plasma and cells the next morning.

In the fourth case the reaction was severe. The patient was semi-comatose and unable to talk. The blood showed an extremely low sugar content, and the corpuscular sugar was not measured. The patient was immediately given 200 cc of orange juice and 5 per cent dextrose rectally. All symptoms and signs disappeared during the next two hours. The blood sugar rose to a normal level, and the patient recovered. The data for these four patients are given in detail in table 1.

Reduction of corpuscular glucose without an abnormally low whole blood sugar was noted in the blood of two of the other four patients. There were two periods of cytglycopenia in the patient who had a lipoma excised from the shoulder, one occurred twenty-nine hours and

TABLE 1—*Blood Sugar Determinations on Four Patients on Whom Thyroidectomies Were Performed*

Case	Date 1926	Hours Post-operative	Blood Sugar Per centage	Plasma Sugar Per centage	Cell Sugar Per centage	Cells Per centage	Serum Per centage	Remarks
1	1/29	30	0.161	0.166	0.150	32	67	Slight reaction
	1/30	48	0.166	0.129	0.044	27	73	
	2/1	103	0.143	0.154	0.113	27	73	
2	3/29		0.142	0.173	0.124	43.4	56.6	Preoperative
		6	0.175	0.195	0.135	33.6	66.4	Normal postoperative
	3/30	22	0.161	0.161	0.161	36.6	63.4	course
		30	0.159	0.155	0.166	34.8	65.2	
	3/31	47	0.146	0.079	0.285	72.4	27.6	
	4/1	71	0.163	0.154	0.180	34.3	65.7	
3	4/12	72	0.110	0.125	0.047	28	72	Mild reaction
	4/13	97	0.131	0.139	0.117	26.5	73.5	
4	3/8		0.09					Severe reaction
	3/10	48	0.025					
	3/12	96	0.10					

the other fifty-three hours after operation. In the other patient there was only one such period fifty hours after a bilateral femoral humerectomy had been performed.

It is interesting to note that even with such low concentrations of corpuscular glucose no symptoms were felt except hunger and no abnormal physical signs were found. This is so contrary to the reaction following a large dose of insulin that it is worthy of notice. As has been shown elsewhere¹ the symptoms and signs of insulin reactions appear when the corpuscular glucose has been reduced to about 10 mg per hundred cubic centimeters. This is true regardless of the levels of the whole blood and plasma sugar at that time; they may be high or low while the reaction is taking place. It is significant that the four patients complained of hunger at the time the corpuscular glucose concentrations were low. Each patient had had a long period of general anesthesia and had gone forty-eight hours preoperatively without any of carbohydrate. Hunger is frequently the first symptom of hypoglycemia.

beginning of an insulin reaction. We believe that the cause of the hunger sensation in our patient is the same as that in the patient experiencing an insulin reaction, namely, a reduction of glucose in the cells of the body tissue, of which the measured corpuscular glucose concentration is an index. The work of Macleod³ on the relation of fixed tissue cell sugar to the onset of insulin reactions furnishes evidence which strongly supports this opinion.

The cause of the symptoms and signs in the patients on whom thyroidectomies were performed is probably the same—a lowered cellular sugar content throughout the body. The underlying physiologic

TABLE 2—*Blood Sugar Determinations on Four Patients Following Operations*

Case	Date	Hours Post oper- ative	Blood Sugar Per centage	Plasma Sugar Per- centage	Cell Sugar Per- centage	Cells Per- centage	Serum Per centage	Remarks
Excision Lipoma								
1	1/12	0	0.110	0.097	0.125	45.7	54.3	Preoperative
		5	0.153	0.163	0.128	38	62	
	1/13	22	0.161	0.160	0.162	40	60	Liquid diet
		29	0.108	0.138	0.058	37.5	62.5	Hunger
	1/14	45	0.173	0.180	0.160	36.2	63.8	
		53	0.113	0.177	0.017	40	60	Hunger
	1/15	77	0.152	0.120	0.212	34.5	65.5	
	1/17	120	0.104	0.124	0.071	38	62	
Femoral Hemorrhaphy								
2	1/15	0	0.120	0.120	0.120	44.4	55.6	Preoperative
		7	0.127	0.110	0.142	46.6	53.4	
	1/16	25	0.144	0.129	0.161	45.7	54.3	Liquid diet
	1/17	50	0.132	0.182	0.057	40	60	Hunger
	1/18	72	0.164	0.181	0.139	40.4	59.6	
	1/20	121	0.124	0.143	0.093	38	62	House diet
Hemorrhaphy								
3	1/26	0	0.119	0.132	0.097	38	62	Preoperative
	1/28	48	0.132	0.138	0.123	40	60	Normal postoperative
		55	0.113	0.113	0.113	36	64	course
	2/ 1	157	0.168	0.177	0.152	36	64	
Cholecystectomy								
4	2/ 5	0	0.106	0.105	0.107	38	62	Preoperative
		7	0.164	0.202	0.104	38	62	Normal postoperative
	2/ 6	24	0.159	0.159	0.159	33	67	course
	2/ 8	78	0.155	0.168	0.123	29	71	

mechanism may be slightly different. These patients have had a high metabolic rate for a considerable period, have lost much weight and have probably seriously depleted their stores of glycogen. The sudden increase in metabolism incident to manipulating the thyroid gland during and shortly after the operation may cause a temporary excessive burning of carbohydrates which cannot be met by glycogenolysis from the already depleted liver and muscle stores, hence the low general tissue sugar, low corpuscular sugar and the associated insulin-like reactions. In this connection it is of interest to note that the patient who did not

3 Macleod, J. J. R. The Problem of the Fundamental Action of Insulin. *Canad. M. A. J.* 15:476 (May) 1925.

have any symptoms after thyroidectomy was in a good state of nutrition. The other three patients who had reactions were thin, underweight and obviously in a poor nutritional state.

SUMMARY AND CONCLUSIONS

Some of the symptoms and signs of postoperative reactions are caused by a depletion of sugar in the tissues, a cytopenia. They may or may not be associated with a hypoglycemia, by that term a low whole blood sugar is meant.

A method is presented which enables one to gain some insight concerning the amount of glucose in the tissues by studying the concentration and distribution of glucose in the blood plasma and erythrocytes.

If methods of study are limited to the one of determinations of whole blood sugar, much useful information concerning carbohydrate utilization will be overlooked.

THE VARYING DEGREES OF ANEMIA PRODUCED BY CARCINOMA IN DIFFERENT PARTS OF THE COLON*

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In 1913 and 1921 W J Mayo¹ called attention to the fact that carcinoma of the proximal half of the colon has a greater tendency to the production of anemia than carcinoma of any other part of the body with the exception of the median portion of the stomach. As this observation gives rise to a number of interesting questions, many of them of considerable clinical importance, it seemed worth while to follow it up with a statistical analysis to see, first, how definite the peculiarity is, and, second, what explanation can be found for it.

For the purposes of this study, we have gone over the records of most of the cases of cancer of the colon in which operation was performed at the Mayo Clinic during the last twenty years and have divided these cases into a number of groups according to the situation of the tumor, the sex of the patient, the number of red cells and the percentage of hemoglobin in the blood (Dare method). The frequency distributions with the corresponding means (or averages) will be found in tables 1, 2 and 3. The trend of the means is shown in chart 1 where the relation between the degree of anemia and the situation of the tumor in the bowel stands out strikingly.

Chart 2 shows in another, and perhaps more convincing way, the difference in the severity of the anemia with cancer in the right and left halves of the colon. There it may be noted how much more frequently low hemoglobin readings of from 30 to 50 per cent are found with tumors on the right side. Without these big differences in the distribution curves we might have felt some doubt about the reliability of the averages because, as is well known, the Dare hemoglobinometer

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1 Mayo W J. Some of the Disputed Problems Associated with Surgery of the Large Intestine, *Am J M Sc* **145** 157-161, 1913, Pernicious Anemia with Special Reference to the Spleen and the Large Intestine, *Ann Surg* **74** 355-359 (Sept) 1921

is not an exact instrument, the laboratory worker has generally to take the mean of two or three readings on the same sample and these estimates vary through a range of 5 per cent or more. Fortunately, however, when 100 such means are averaged negative errors tend to balance positive ones and the first two figures in the result become quite trustworthy. If doubts had remained we would have based our

TABLE 1—*Red Cell Counts and Hemoglobin Readings with Carcinoma in Different Parts of the Colon*

Red Cells, Millions	Cecum		Ascending Colon and Hepatic Flexure		Transverse Colon		Descending Colon and Sigmoid Flexure		Sigmoid		Rectum	
	Men	Women	Men	Women	Men	Women	Men	Women	Men	Women	Men	Women
1 500-1 999	1										1	
2 000-2 499	2						1					
2 500-2 999	2	3	4	1	1		1		1		1	
3 000-3 499	6	5	10	7	3	3				1		
3 500-3 999	9	9	19	12	13	4	10	4			11	1
4 000-4 499	14	9	24	8	17	8	17	15	20	24	30	
4 500-4 999	6	10	17	6	7	3	17	7	22	7	47	
5 000-5 499	2	2	3	1	3		2					
5 500-5 999							1			2		
6 000-6 499				1								
Totals	42	38	77	5	48	19	46	27	62	40	114	2
Mean	3 893	4 066	4 038	4 055	4 073	4 118	4 294	4 196	4 877	4 200	4 134	4 180
S. D.	774	672	610	670	572	511	490	615	410	84	177	110
P. I. of mean	80	70	90	60	60	80	50	60	40	60	60	60
Hemoglobin, per Cent												
0-34	3	5		1	2						2	
35-39	5	5	5	4	4	1					1	
40-44		1	9		6	1	7	2				
45-49	7	3	9	1		2				1		1
50-54	2	4	10		1	2	2		4	1	2	
55-59	4	5	8	5	6	2	8	5		4		
60-64	9	1	7	7	3					4		
65-69	2	5	11	4	6	1		7	10		3	
70-74	7	13	17	7	13		11	1		17	10	
75-79	11		15	5	3	4	10	4				
80-84	6	3	5	2	2	4	6	6				
85-89	2	2	4									
90-94	1									1	1	
95-99	1			1			1					
Totals	63	70	99	1	2	21	60	60	7			
Mean	63.5	69.6	61.9	64.1	61.6	67	67.6	67.6	70.6	71		
S. D.	16.8	16.5	14.4	15.2	15.4	11	14.7	14.1	16.6	11		
P. I. of mean	14	16	16	14	14	21	12	12	16	16		

In the table and in tables 2 and 3 S. D. is standard deviation and P. I. is probable error.

arguments on the gradation in the averages of the red cell counts parallel those of the hemoglobin readings and which doubtless of high degree of accuracy because they are based on determinations by trained technicians, experts in the use of a standard color scale and precision. Finally, it can be shown with a great deal of probability that the chances are 500 to 1 that the error in the averaged red cell count exceeds one per cent.

Cecum	Ascending Colon and Hepatic Flexure	Transverse Colon	Descending Colon and Sigmoid
Percent	Percent	Percent	Percent

Hemoglobin per Cent	Cecum		Ascending Colon and Hepatic Flexure		Transverse Colon		Descending Colon and Splenic Flexure		Sigmoid		Rectum		Total Right Colon		Total Left Colon		Total Colon	
	Cases	Per Cent	Cases	Per Cent	Cases	Per Cent	Cases	Per Cent	Cases	Per Cent	Cases	Per Cent	Cases	Per Cent	Cases	Per Cent	Cases	Per Cent
20-24	8	71	4	27	2	26	1	08	2	16	1	04	12	46	1	02	1	01
25-29	10	89	9	60	5	65	5	42	1	08	1	17	19	72	3	06	17	21
30-34	1	35	12	80	7	91	5	42	5	41	3	13	16	61	1	02	25	31
35-39	10	89	10	67	5	65	13	109	6	49	9	38	20	76	15	31	38	46
40-44	6	53	15	100	3	39	12	101	6	49	3	13	21	80	9	19	34	42
45-49	9	80	13	87	8	96	9	76	16	130	11	47	22	84	19	40	43	53
50-54	10	89	14	93	6	78	24	202	44	358	18	76	24	91	22	41	52	64
55-59	7	62	15	100	7	91	21	168	30	244	72	406	22	84	29	61	30	72
60-64	20	177	20	133	16	208	12	101	10	81	14	59	40	152	43	90	72	88
65-69	14	124	23	153	7	91	6	50	2	16	3	13	37	141	164	343	220	299
70-74	9	80	7	47	6	78	1	08	1	08	1	04	16	61	36	75	163	203
75-79	1	35	7	47	5	65	1	08	1	08	1	04	11	42	23	58	27	33
80-84	1	09	1	07	1	65	1	08	1	08	1	04	2	08	2	04	3	04
85-89	1	09	1	07	1	65	1	08	1	08	1	04	2	08	2	04	3	04
90-94	1	09	1	07	1	65	1	08	1	08	1	04	2	08	2	04	3	04
95-99	1	09	1	07	1	65	1	08	1	08	1	04	2	08	2	04	3	04
Total	113	150	77	119	123	236	263	475	815	706	106	03	673	135	03	03	03	03
Mean	62.2	62.6	63.1	67.1	71.5	71.9	71.9	71.9	71.9	71.9	71.9	71.9	71.9	71.9	71.9	71.9	71.9	71.9
SD	16.7	15.1	15.4	13.8	8.8	9.7	9.7	9.7	9.7	9.7	9.7	9.7	9.7	9.7	9.7	9.7	9.7	9.7
Mean duration of symptoms, months	11	08	12	09	05	05	05	05	05	05	05	05	05	05	05	05	05	05
Mean duration, days	114	117	110	80	100	100	100	100	100	100	100	100	100	100	100	100	100	100
Loss of weight, pounds	27	30	27	25	27	27	27	27	27	27	27	27	27	27	27	27	27	27
Loss of weight, pounds	244	256	227	245	179	179	179	179	179	179	179	179	179	179	179	179	179	179

	07	256	30	80	100	04	298	673
* The total number of cases of carcinoma of the colon	07	256	30	80	100	04	298	673
transverse colon		08	227	25	27	105	07	106
ascending colon			10	245				03
Descending colon				09	178	20		03
Sigmoid flexure					07	167		
Total						01		

* During the course of the work we analyzed records from 168 cases of carcinoma of the colon forty of the small intestine 203 of the stomach 170 of the breast and 114 of the uterus all removed at operation and studied microscopically

The seventy seven cases of cancer of the large bowel here, some were used for the histo-logical study of the tumor tissue.

TABLE 3.—Percentage Distributions of Hemoglobin with Carcinoma of the Stomach, Small Intestine, Uterus and Breast and Tuberculosis of the Cecum

[illegible]

INTERPRETATION OF DATA

The next question is, What interpretation can be placed on the figures that we have obtained? Assuming that the degree of anemia is dependent largely on the duration of the illness, on the amount of weight lost, on the presence or absence of metastasis, and perhaps on

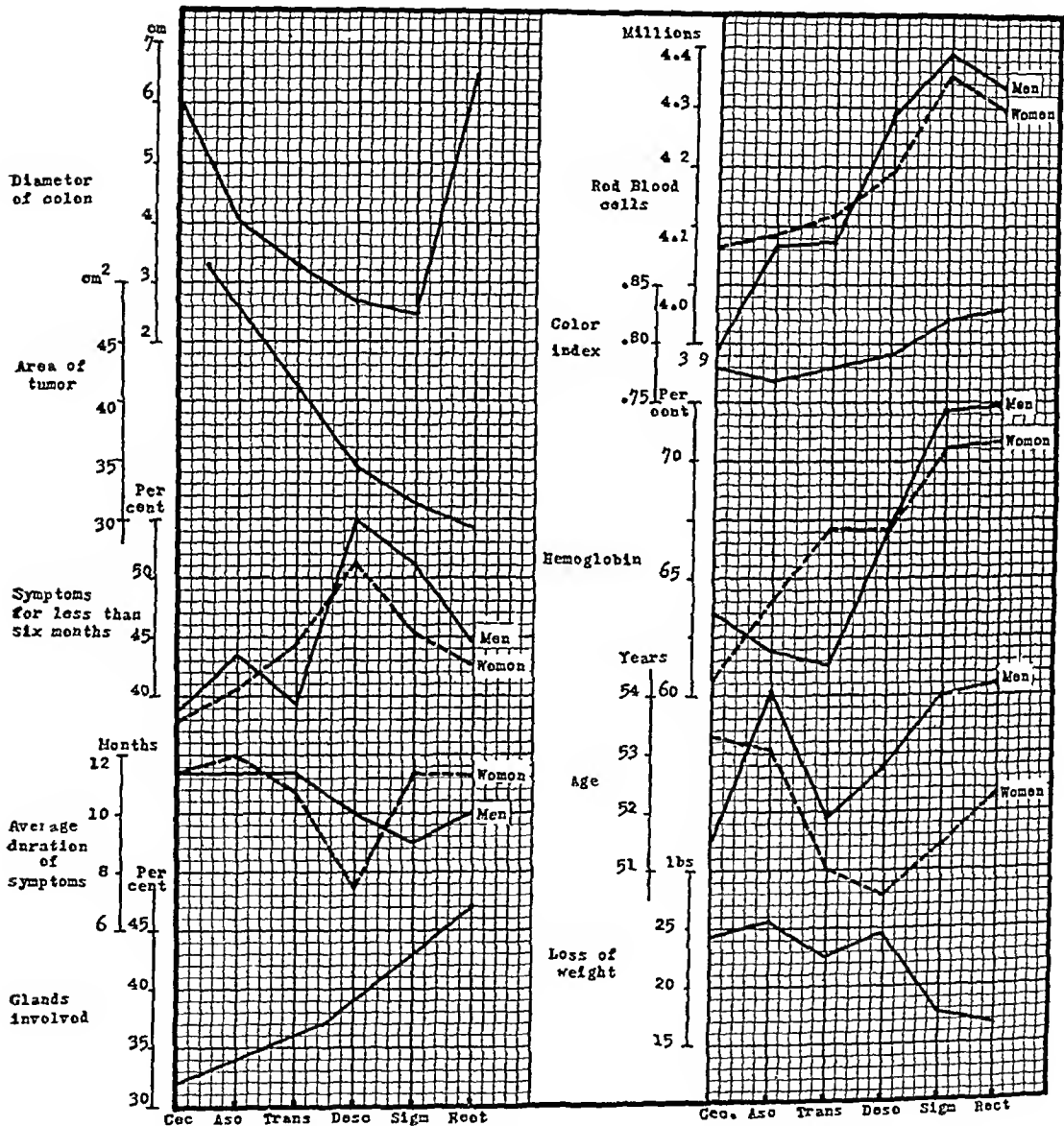
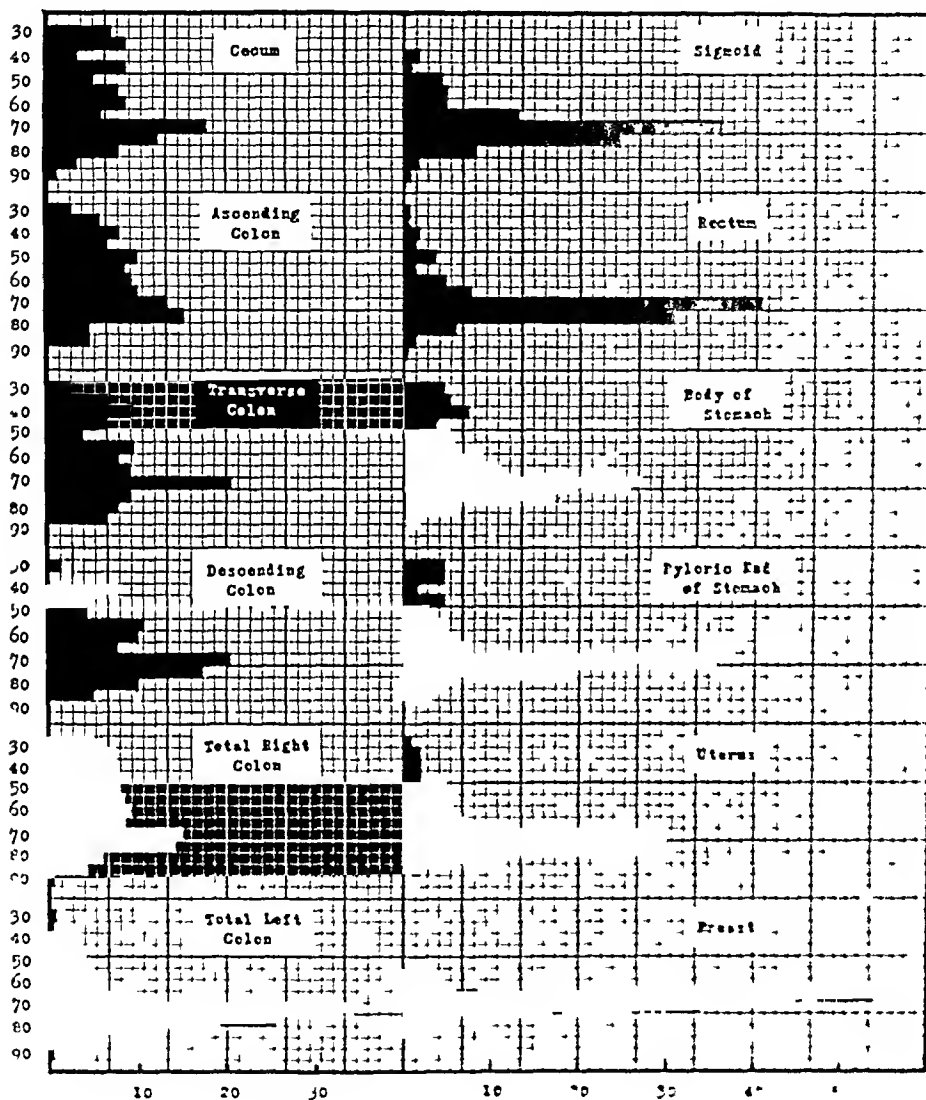


Chart 1—Gradation in several of the groups of data given in the text, the abscissas indicate the different regions from one end of the colon to the other

the age of the patient, might not the differences which we have found be due simply to an unequal distribution in the two groups, of persons who have lost weight who are old, or who have older and more extensive lesions?

In working out the answer to this question our first move was to see if the factors just mentioned really do have any influence on the production of anemia, because if they do not, they can be disregarded and the problem will be greatly simplified. We took therefore all cases of men and women with cancers in any part of the colon and calculated



been inversely proportional to the duration of the symptoms, this figure would have been -1 , and if there had been absolutely no correlation between them, it would have been zero. The coefficient between percentage of hemoglobin and duration of symptoms was -0.131 ± 0.039 for tumors of the right side of the colon, and -0.081 ± 0.063 for tumors of the left side. As will be seen later, this absence of correlation observed with tumors on the left side is probably due to the fact that the first symptoms are likely to be those of obstruction, while with tumors on the right side, obstruction comes later and there is time for the development of anemia, the severity of which will be somewhat related to the duration of the symptoms.

The coefficient between the red cell count and the amount of weight lost was 0.153 ± 0.026 . For cell count and age, the coefficient was 0.028 ± 0.035 which shows that there is no relation. Strange to say, there was no relation between duration of symptoms and loss of weight, the factor being 0.047 ± 0.030 . As will be seen later, the main reason for this is probably that the duration of symptoms is a poor index to the age of the tumor.

With such low correlation coefficients we can now say that no allowance need be made for differences in the ages of the patients or in the amount of weight lost. This is all the more true because as may be seen from chart 1, these two factors vary little anyway. The only significant difference is found with tumors of the sigmoid and rectum in which the loss of weight is not so great as with tumors in the rest of the colon.

Unfortunately, we cannot put much confidence in the coefficient for the duration of symptoms and degree of anemia, because it is certain that the onset of symptoms marks, not the beginning of cancerous growth, which is really what we would like to determine, but the time when the mass has developed to a point where it can interfere with the passage of fecal material through the bowel. This feature will be discussed later in more detail.

COMPARATIVE MALIGNANCY

When confronted with the differences in the production of anemia associated with tumors in the various parts of the colon, one of the first things to be thought of is a corresponding and underlying difference in the extent of metastasis. A little study showed, however, that even if such a difference were present it could not account for the gradation in anemia, because in patients still suitable for operation—the type that we have studied—the spreading of the growth has little influence on the blood and the difference in the production of anemia with tumors in the right and left halves of the colon can be shown just as well in the group without metastasis as in the group with it (table 4).

Even with this proof the thought remained in our minds that tumors of the right side of the colon might still in some way have a greater malignancy, so we turned to the careful investigation of this subject carried out by Craig and MacCarty-Haves⁷ and McNay.⁸ They picked off and studied microscopically the glands removed with 300 segments of the colon resected for cancer, and found a gradation in the tendency of these tumors to metastasize, but it was just opposite to that which would be needed to explain the gradation in the production of anemia. There was more or less involvement of the regional glands in 47 per cent of the rectal and in 32 per cent of the cecal cases, and a fairly even gradation in metastasis with the tumors situated in the regions between.

The high degree of anemia with colonic cancers can hardly be ascribed to a high degree of malignancy, because it is well known that such tumors are generally of low malignancy and that they metastasize

TABLE 4—*Influence of Metastasis on the Red Cell Counts and Hemoglobin Readings*

	Carcinoma Without Metastasis				Carcinoma With Metastasis			
	Cases	Right Colon	Cases	Left Colon	Cases	Right Colon	Cases	Left Colon
Red cells, millions	195	4.012 \pm 0.06	426	3.779 \pm 0.062	40	3.573 \pm 0.07	7	3.400 \pm 0.04
Hemoglobin, per cent	272	62 \pm 0.70	486	70.7 \pm 0.9	40	61.7 \pm 1.0	1	60.0

slowly as compared with those in the stomach. With gastric cancers MacCarty and Blackford⁹ found involvement of the regional glands in fifty-two of one hundred cases studied.

THE GRADATION IN THE DIAMETER OF THE BOWEL

The most probable cause for the gradation in anemia seems to be the gradation in the diameter of the bowel. On measuring a few roentgenograms of the colon, we found that the diameter of the cecum is about 6 cm, that of the ascending colon, 4 cm, of the transverse colon, 3.3 cm, of the descending colon, 2.7 cm, of the sigmoid, 2.5 cm, and of the rectum, 6.5 cm. As has already been pointed out, the first symptoms of cancer of the colon are ordinarily those of obstruction, in other words, the tumor generally grows silently until it becomes large enough to interfere with the passage of the fecal material. Under those circumstances one should expect the size of the tumors to be graded from the descending colon to the cecum because the onset of urgent symptoms would mean simply that a certain proportion of the lumen had become blocked. A tumor the size of a walnut, which would produce serious symptoms if situated in the descending colon, would pass unnoticed in the cecum, while a tumor as large as the palm of the hand, which might cause some pain and anemia in the cecum, would be incompatible with life if transplanted to the descending colon.

Furthermore, the cecum would be more likely to tolerate a large tumor because its contents are fairly liquid and more likely to slip past a growing obstruction. An exception to this rule must of course be made for those growths which begin near the ileocecal sphincter. They soon cause obstruction in the small intestine, and they act more like ileal than cecal tumors. In one such case in which the sphincter alone was affected, death followed a stormy illness of only six months' duration.

GRADATION IN THE SIZE OF THE TUMORS

If the foregoing argument is correct, there should be a gradation in the size of the tumors in the different parts of the bowel and, as may be seen in table 5 and chart 1, that is just what was found. The surface areas of the tumors in square centimeters ranged from 51.6 ± 2.0 in the cecum to 29.1 ± 1.3 in the rectum. The only difficulty that remains is that, according to our theory, the rectum, with its large diameter, should have tumors larger than those in the descending colon. Actually they averaged a little smaller, but this need not disturb us greatly because a number of facts have appeared during this analysis, all suggesting that cancers of the rectum, and perhaps of the sigmoid, should be studied under a separate classification, apart from those in the rest of the colon. This may be due to differences in the structure of that part of the tube, to differences in its relation to surrounding organs, to the special nerve supply, and to its nearness to the outside of the body, which probably causes such symptoms as the discharge of blood and pus to be observed earlier than they would be if the tumor were higher up.

DURATION OF SYMPTOMS

If our theory is correct there should also be a gradation in the duration of symptoms because with tumors of the left side of the colon obstruction should appear early, the symptoms should be acute and urgent and the patient should be driven to seek relief early. With tumors of the cecum not involving the ileocecal sphincter obstruction should come late and there should be more time for the development of symptoms such as indigestion, weakness and anemia all of which a patient might be able to neglect for a while.

Actually while 54 per cent of the patients with cancer of the narrow descending colon felt sick enough to come to the clinic with

TABLE 5—*Site of Resected Tumors*

Area in Sq. Cm.	Cecum and Ascending Colon		Transverse Colon		Descending Colon		Sigmoid and Recto-sigmoid		Anus		Stomach	
	Cases	Per Cent	Cases	Per Cent	Cases	Per Cent	Cases	Per Cent	Cases	Per Cent	Cases	Per Cent
Up to 10	6	5.7	3	8.4	5	10.0	10	14.7	2	3.0		
11-20	10	9.4	8	22.2	6	20.0	10	14.7	3	4.5		
21-30	16	15.1	5	14.9	6	20.0	15	21.1	10	15.0		
31-40	15	14.1	6	16.7	5	10.0	8	11.8	1	1.5		
41-50	18	17.0	5	14.4	5	10.0	7	10.0	8	12.0		
51-60	7	6.6	4	11.2	5	16.7	5	7.4				
61-70	8	7.5	1	2.8		10.0	4	5.9	4	6.0		
71-80	6	5.7	2	5.6	1	3.3	4	5.9			1	1.5
81-90	6	5.7	1	2.8			1	1.5				
91-100	4	3.8									4	6.0
101-110	2	1.9	1	2.8								
111-120	1	0.9	1	2.8					1	1.5		
121-130	4	3.8	1	2.8							1	1.5
131-140	1	0.9										
141-150	1	0.9										
151-160											1	1.5
161-170	1	0.9										
Total	100		36		51		66		20		6	
Mean		40		41.5		44.5		41.5		30		30
S.D.		1.0		0.0		0.0		1.0		1.0		1.0
P.D. of mean		2.0		4		4		1.5		1		1

was found at the time of operation. In other cases the disappearance after operation of symptoms of indigestion which had been present for years left us with the strong impression that the tumor either must have existed for a long time or had developed in an old stricture, polyp or diverticulum. Actually, in a few cases a primary polyp or diverticulum could still be identified at the time of operation. As we did not feel justified in using the twelve and fifteen-year histories in making the averages, and as a line had to be drawn somewhere, we put it at six years.

CANCER OF THE SMALL INTESTINE

As was to be expected from our hypothesis, cancer in the narrow and more irritable small bowel produced urgent symptoms even more promptly than in the descending colon, and 64 per cent of the patients seen at the Mayo Clinic with such growths applied for relief within six months after the onset of the trouble. The average duration of the illness was 7.7 ± 0.9 months, and none of the patients had symptoms for more than three years.

MODE OF ACTION OF THE TUMOR ON THE BLOOD

It appears, then, that the graded difference in the production of anemia is associated with a gradation in the size and age of the tumors which, again, is due to a gradation in the diameter of the colon. As the regression seemed to be nonlinear, on Dr. Dunn's advice, we divided the correlation table into two parts, the first one including cases with hemoglobin contents up to 50 per cent and the other with hemoglobin over 50 per cent. In the first group the correlation factor was -0.485 ± 0.01 , and in the second it was -0.319 ± 0.073 . These coefficients are definite and twice as large as any of the other coefficients that we have computed.

The next question is, How does the tumor act on the blood? Does it elaborate hemotoxins, does it destroy a particularly important area of the mucous membrane of the bowel, does it act by producing obstruction, or does it act by producing a large ulcerated surface from which the body can lose blood and other poorly replaceable fluids and through which it can absorb bacterial poisons?

In order, first, to study the influence of cancer alone, without the complication of a bleeding, oozing and infected surface, we analyzed the records of 130 patients with nonulcerating cancer of the breast, operated on at the clinic. The hemoglobin readings were practically normal for the Dare instrument and the average was 74.4 ± 0.2 per cent. The average red cell count was $4,410,000 \pm 20,000$ (chart 2). The tumors ranged in size from 5 to 90 sq. cm. with an average of 8.4 ± 0.6 sq. cm. There was absolutely no correlation between the size of the

tumor and the hemoglobin reading but this may not mean much because most of the tumors were apparently too small to have any effect on the blood.

Similarly, the average hemoglobin reading in fifty-five women with carcinoma of the fundus of the uterus not associated with profuse bleeding was 74.9 ± 0.6 per cent. All but 10 per cent of these women had hemoglobin readings over 70 per cent. Twenty-seven women with the same type of cancer in the fundus but with considerable bleeding had an average hemoglobin of 61.8 ± 1.8 per cent which shows how important the factor of hemorrhage is. Similarly, twenty-six women with cancer of the cervix without much hemorrhage had an average hemoglobin of 79.2 ± 0.9 per cent while twenty women with the same type of cancer and with hemorrhage had an average of 64.5 ± 2.6 .

The inability of carcinomatous tissue alone with little or no bleeding surface to lower the amount of hemoglobin in the body was shown in a number of cases in which the condition of the blood returned up to normal in spite of the fact that a large cancer of the bowel had been short-circuited and left. In one such case the patient returned with a big brown mass involving the anterior abdominal wall, but yet the hemoglobin reading was considerably higher than it had been a year before when she came with a small napkin-ring-type of growth. In another case a woman with a small carcinomatous ulcer of the rectum had a liver so full of metastatic nodules that it reached to the umbilicus and at necropsy weighed 5,600 Gm. The hemoglobin reading was 67 per cent. We must conclude therefore that the mass of the cancer cells is not the important factor in producing anemia.

which there was little pulmonary involvement but a great deal of change in the cecum, and found an average hemoglobin reading of 74.3 ± 0.9 per cent

All this evidence makes it appear improbable, then, that there is any function of the cecal mucous membrane which is essential to the maintenance of normal conditions in the blood. It does not, of course rule out such a possibility, and we do not feel like putting aside lightly the clinical impressions of men of enormous experience. It should be noted, however, that if we ascribe such peculiarities to the mucous membrane of the cecum, we may with perhaps greater propriety ascribe them to the mucous membrane of the stomach, where the degrees of anemia produced by small tumors almost equal those produced in the cecum by very large ones.

THE FACTOR OF OBSTRUCTION

The striking improvement in the condition of the blood and general health which occurs in many cases after the removal or short-circuiting of narrow "napkin-ring" tumors of the transverse and descending colon makes it appear as if obstruction of the bowel must play a large part in lowering the vitality of the body. The same type of improvement is seen also after the short-circuiting of noncancerous lesions of the bowel. We noted one case of a young man aged 23 who had had severe indigestion and abdominal pain for two years. The hemoglobin reading was 65 and the red cell count was 3,830,000. Two months later, after a large inflammatory mass in the cecum had been short-circuited, the hemoglobin percentage had risen to 72 and the red cell count to 4,720,000. In another case a big tuberculous mass involving the cecum was short-circuited and left. Two years later the hemoglobin reading was 72 per cent and the red cell count was 4,780,000. In these cases there is generally a good deal of shrinkage in the tumor immediately after the operation but that can hardly account for all the improvement.

Against the idea that chronic obstruction is largely responsible for the anemia is the finding of normal hemoglobin and a normal blood count in the case of the woman already mentioned who had suffered for six months with symptoms of obstruction so fulminant that she finally died in one of the attacks before she could be operated on. In this case the effect of obstruction could be studied almost by itself because the growth was a small one limited sharply to the region of the ileocecal valve.

THE IMPORTANT FACTORS IN THE PRODUCTION OF ANEMIA

One thing we can say and that is that the passage of feces over the tumor, whether cancerous or tuberculous, has a great deal to do with the production of anemia and cachexia. And that leads up to our final

which the disease either was extensive, reaching into the first part of the transverse colon, or else associated with considerable hemorrhage

SUMMARY

Carcinoma of the cecum and ascending colon has a marked tendency to produce severe grades of anemia. This tendency is progressively less marked with cancers of the transverse, the descending, and the pelvic portions of the colon.

The gradation cannot be explained on the basis of a greater loss of weight, more severe hemorrhage, or greater malignancy of the tumors in the right half of the colon. The malignancy of colonic cancers as a whole is low as compared with that of gastric cancers, and the tendency to metastasize is greater with cancer of the rectum than with that of the cecum.

The cause for the gradation in anemia seems to be a gradation in the surface area of the tumors, from an average of 51.6 ± 2.0 sq. cm. in the cecum to 31.2 ± 1.7 sq. cm. in the sigmoid. This gradation is dependent, again, on a gradation in the diameter of the colon from about 6 cm. in the cecum to 2.5 cm. in the sigmoid. The patient seeks relief when the lumen of the bowel becomes more or less blocked. In the descending colon this can happen when the tumor has grown to the size of a walnut, in the cecum it does not happen until the mass is as large as a man's hand.

As would be expected, then, the patients with cancers in the narrow descending colon are driven to seek relief early, usually within six months after the onset of the trouble. The symptoms with cancer of the cecum are less urgent and the sufferers often put off consulting a physician until they are markedly anemic.

There is a definite relation between the area of the tumor removed at operation and the degree of anemia.

The cancer cells alone do not seem to have much effect on the blood, as shown by the fact that nonulcerating carcinoma of the breast or fundus of the uterus is seldom associated with anemia, that the blood of patients with large cancers of the bowel which have been short-circuited and left often returns for a while almost to normal, and that patients with insignificant cancers of the bowel and enormous masses of cancer tissue in the liver show only moderate grades of anemia.

The anemia with cancer of the cecum cannot be ascribed to the loss of an essential mucous membrane or function because the blood picture usually reverts almost to normal after that part of the bowel has been short-circuited or removed. Furthermore, its destruction by tuberculosis is ordinarily not associated with much anemia.

The essential factor in the production of anemia seems to be the presence of a large ulcerated area from which blood can ooze and through which bacteria can enter. Nowhere else on the inside of a body can ulcerating cancers be found so large as in the cecum, and nowhere else are such big raw surfaces in contact with a concentrated culture of organisms, many of them virulent, and when injected into animals capable of producing severe anemia.

These observations emphasize the necessity for looking primarily at the cecum when a patient presents himself with marked secondary anemia and few symptoms to point to the source of the trouble. It should be remembered also that with carcinoma of the colon the presence of marked anemia is not the same contraindication to operation as it is in the case of carcinoma of the stomach.

PORTAL CIRRHOSIS WITH ASCITES AND ITS SURGICAL TREATMENT

A REVIEW OF TWENTY-SIX CASES *

WALTER HUGHSON, M D

BALTIMORE

Few diseases approached from a surgical standpoint offer so many interesting possibilities for individual ingenuity and at the same time oppose so many difficulties to rational treatment as does portal cirrhosis with ascites. The stage of the disease under discussion in most instances probably is the last stage, and the surgeon's efforts are directed toward the correction of this particular manifestation, though he is not given an opportunity to affect the disease itself. The literature on the subject is remarkably voluminous when one considers the comparative rarity of the condition and also the fairly brief period—now thirty years—during which surgical operation has been used as a method of treatment. Isolated reports of cases in which treatment consisted of the various surgical procedures available appear with considerable regularity, and in the main these reports seem to indicate a certain justification for surgical intervention. In view of the human tendency to announce or at least to emphasize only favorable results, a moderate degree of skepticism might temper somewhat the first feeling of optimism. There can be little doubt that the situation is not entirely satisfactory from a surgical standpoint. Cures, as estimated by the permanent disappearance of fluid, are certainly infrequent, and the surgeon who can report definite improvement in a number of cases may regard himself as fortunate.

Were the diagnosis of portal cirrhosis a simple matter, statistics as to the results of surgical treatment would be of much greater value than they are at present. Surprisingly little attention is paid to this important phase of the subject. Direct inspection of a liver may tend to confirm the belief that cirrhosis does exist, but such evidence is by no means conclusive. Microscopic examination of a biopsy specimen is the only method by which an absolute diagnosis can be made during life. In only one report reviewed by the author has such positive evidence been recorded on microscopic examination. Even autopsy observations are seldom tabulated in support of a clinical diagnosis. Great confusion seems also to exist in the classification of cirrhotoses of the liver. Cirrhosis is a general disease of which there are many distinct varieties. A definite etiology can be ascribed to some types but not to others.

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There should be no uncertainty as to the type for which procedures may be used with some hope of success. Further will be placed on this particular point in the discussion of the herewith reported

Though this particular type of cirrhosis is described in all text and in many special articles on the subject for the sake of clear statement of the pathology, etiology, diagnosis and methods of treatment will be presented. I shall not attempt to offer a review of the literature, as several monumental articles are available, notably that of Hopfner.¹ Though such compilation an extremely useful purpose in the matter of reference the it what to confuse further an already uncertain situation.

DEFINITION OF TERM PORTAL CIRRHOSIS

Portal cirrhosis as defined in Osler's *'System of Medicine'* "chronic degenerative and inflammatory disease of the liver characterized by recurring degeneration and regeneration of the hepatic chyma and by concomitant and consecutive fibrosis in interlobular or portal spaces all of which leads ultimately to ob of the portal circulation." In Barker's *'The Clinical Diag Internal Diseases,'* volume 2 the following statement is a reference to portal cirrhosis of the liver:

Under this heading I shall include (1) *ordinary portal cirrhosis* (or *atrophic cirrhosis* of Lieberkuhn) (2) *Banti's disease* or cirrhosis with (3) the cirrhosis of *hemochromatosis* and (4) *Alcohol cirrhosis* of the liver with progressive degeneration of the nucleus hepaticus.

In all forms of portal cirrhosis chronic degenerative changes occur in the liver, the connective tissue developing in the interlobular or portal spaces and leading finally to obstruction of the portal circulation and the development of collateral circulations between the venous system and the arterial system.

ETIOLOGY

As is true of so many diseases which are primarily medical and later become surgical for the relief of some particular symptom, physicians are completely in the dark as to the true etiology of portal cirrhosis. With the advance made in medicine and pathology during the past two decades, the originally assigned cause, alcoholism, has fallen into the discard. The familiar term "gin-drinker's liver" was of much greater significance from an etiologic standpoint than "cirrhosis hepatis." A few of the older pathologists still cling to this idea, and recent statistical studies indicate that the incidence of portal cirrhosis appears to be on the decline in certain European countries where true temperance has developed over a period of years. However, as Barker says, "Of late, more stress has been laid upon *intoxications* and *infections* as a cause of cirrhosis hepatis." MacCallum,⁴ in referring to alcohol as the etiologic factor, states that "although it may well play some part, its influence is undoubtedly greatly exaggerated." In a remarkably thorough and painstaking investigation of this phase of the subject, Friedenwald⁵ concluded that "The experimental reproduction in animals of certain of the more characteristic diseases of human beings, attributable to the abuse of alcohol, such as cirrhosis of the liver has not been satisfactorily attained." Much has been done experimentally, but so far little of practical value has been developed. The more important contributions are those of Opie⁶ and others, who have combined bacterial infection with various poisons, such as chloroform, which destroy liver cells, Longcope,⁷ who has produced lesions resembling those found in cirrhosis by repeated anaphylactic shocks caused by injections of egg white or other protein, and Pearce,⁸ who by the injection of hemolytic and hemagglutinative serums caused necrotic lesions and later cirrhotic changes in experimental animals.

Bassler⁹ has made an observation from the clinical standpoint, which if confirmed should prove of importance. He states that in 8 per cent

4 MacCallum, W. G. A Text Book of Pathology, Philadelphia, W. B. Saunders Company, 1924.

5 Friedenwald, J. The Pathologic Effects of Alcohol on Rabbits, J. A. M. A. **45** 780 (Sept. 9) 1905.

6 Opie, E. L. On the Relation of Combined Intoxication and Bacterial Infection to Necrosis of the Liver, Acute Yellow Atrophy and Cirrhosis, J. Exper. Med. **12** 367, 1910.

7 Longcope, W. T. Cirrhosis of the Liver Produced by Chronic Protein Intoxication, J. A. Am. Phys. **28** 497, 1913.

8 Pearce, R. M. Experimental Cirrhosis of the Liver, J. Exper. Med. **8** 64, 1906.

9 Bassler, A. Portal Cirrhosis from a Gastro-Enterological Viewpoint, M. J. & Record **119** 121, 1924.



all connected together into an irregular network, but they have lost their regular relation to the original portal veins, bile-ducts, and hepatic veins

Microscopical study confirms all this. Everywhere in the section there are found patches of liver-cells arranged in a most disorderly fashion. All bear evidence of having been enlarged by the multiplication of their cells, so that the arrangement with reference to portal and efferent veins is all that will tell us whether we have the enlargement of a whole lobule or of an isolated group of cells.

The masses of liver-cells quickly increase in size by multiplication of their cells, new capillaries are formed in every direction, and this labyrinth of cells expands, pressing the stroma away on all sides. For a time

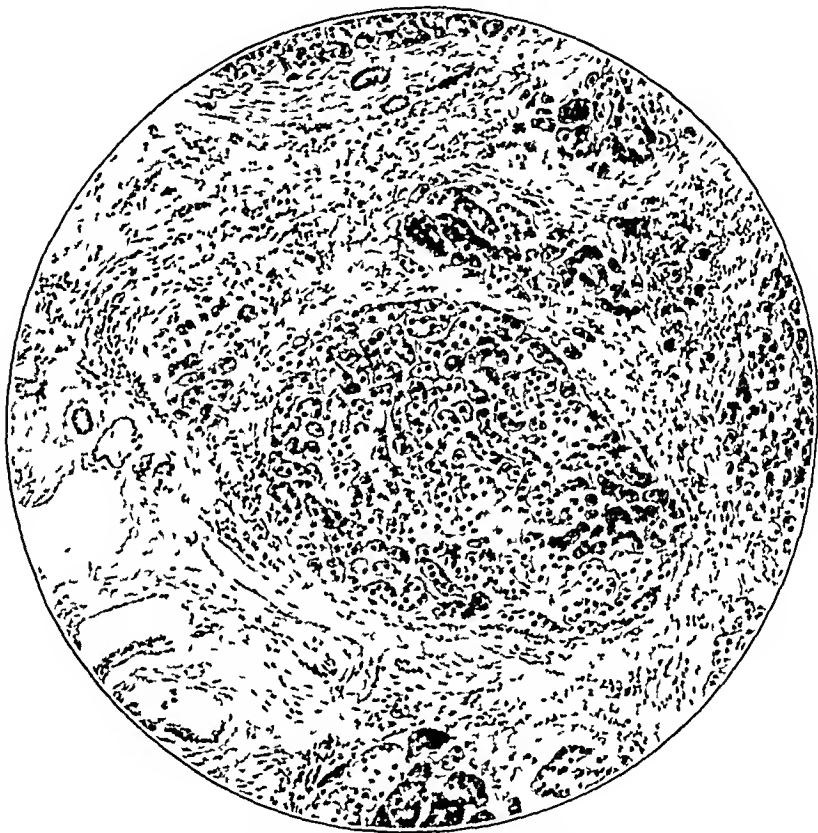


Fig 2—Nodular cirrhosis showing atypical arrangement of liver cells in each nodule and extensive scarring (From MacCallum A Text Book on Pathology)

the liver-cells are normal, but then comes another injury, and many of the hyperplastic nodules are partly destroyed. The whole process is repeated, and not only once, but many times. It is clear that this must lead to an extraordinary distortion of the liver's structure (fig 2).

The pathologic explanation of ascites, the condition for which surgical intervention is really used, is not entirely clear. The progressive cirrhosis described in the foregoing supposedly makes it difficult for the portal blood to pass through the liver, and in consequence the tributaries and branches of the portal vein become greatly distended. This apparent

stagnation of the blood in the portal system impairs the function of the organs drained by it. The spleen becomes enlarged—a condition by no means always found at operation—and digestion is interfered with although here again appears a discrepancy, for the chronic gastritis of a person addicted to the use of alcohol is presumed to be a primary rather than a secondary factor. As a result of this venous stagnation fluid filters into the peritoneal cavity, the ascites thus established tends to persist, and by its presence adds to the burden of the already embarrassed portal circulation.

Here as elsewhere in the body, gradual obliteration of a blood channel, whether arterial or venous, results in the formation of collaterals. The development of such new routes following a venous obstruction is never so efficient as in the case of an artery, owing to the marked differences in blood pressure. However, there are few conditions in which adequate collaterals are not established, unless there is a complete thrombosis of all the veins involved. The collaterals formed in cirrhosis of the liver are extensive, and are well described by Charcot whose diagrammatic representation is shown in figure 3.

One condition associated with cirrhosis and ascites which is seldom referred to is the rather remarkable thickening of the parietal peritoneum. It may be urged that this change occurs in every condition characterized by a chronic peritoneal effusion, yet in no other disease, with the possible exception of a general peritoneal carcinomatosis is this change so striking. In cirrhosis the parietal peritoneum may attain a thickness of from 2 to 4 mm., and on gross examination may appear markedly injected and hyperemic. This fact has considerable significance in view of the well known absorbing properties of normal peritoneum.

DIAGNOSIS

Unfortunately, the clinical diagnosis of cirrhosis of the liver even in the presence of ascites is uncertain. I shall not consider here the diagnosis of the disease before this development becomes manifest when obviously correct interpretations of signs and symptoms must be even more problematic. However indigestion, an enlarged firm liver, splenic enlargement of some degree, pain in the right hypochondrium and a subicteroid tint to the skin and sclera in a person who has led a more or less irregular life suggests possibility of a developing cirrhosis. Actual jaundice is an uncommon symptom and is probably due to some accessory disease. Indications of a developing collateral circulation, hemorrhoids, esophageal varix (hematemesis) and in the later stages mild or severe toxic symptoms add weight to the preliminary diagnosis. The final stage is the development of ascites, or which I prefer to say, comes after the signs of portal obstruction have reached their maximum.

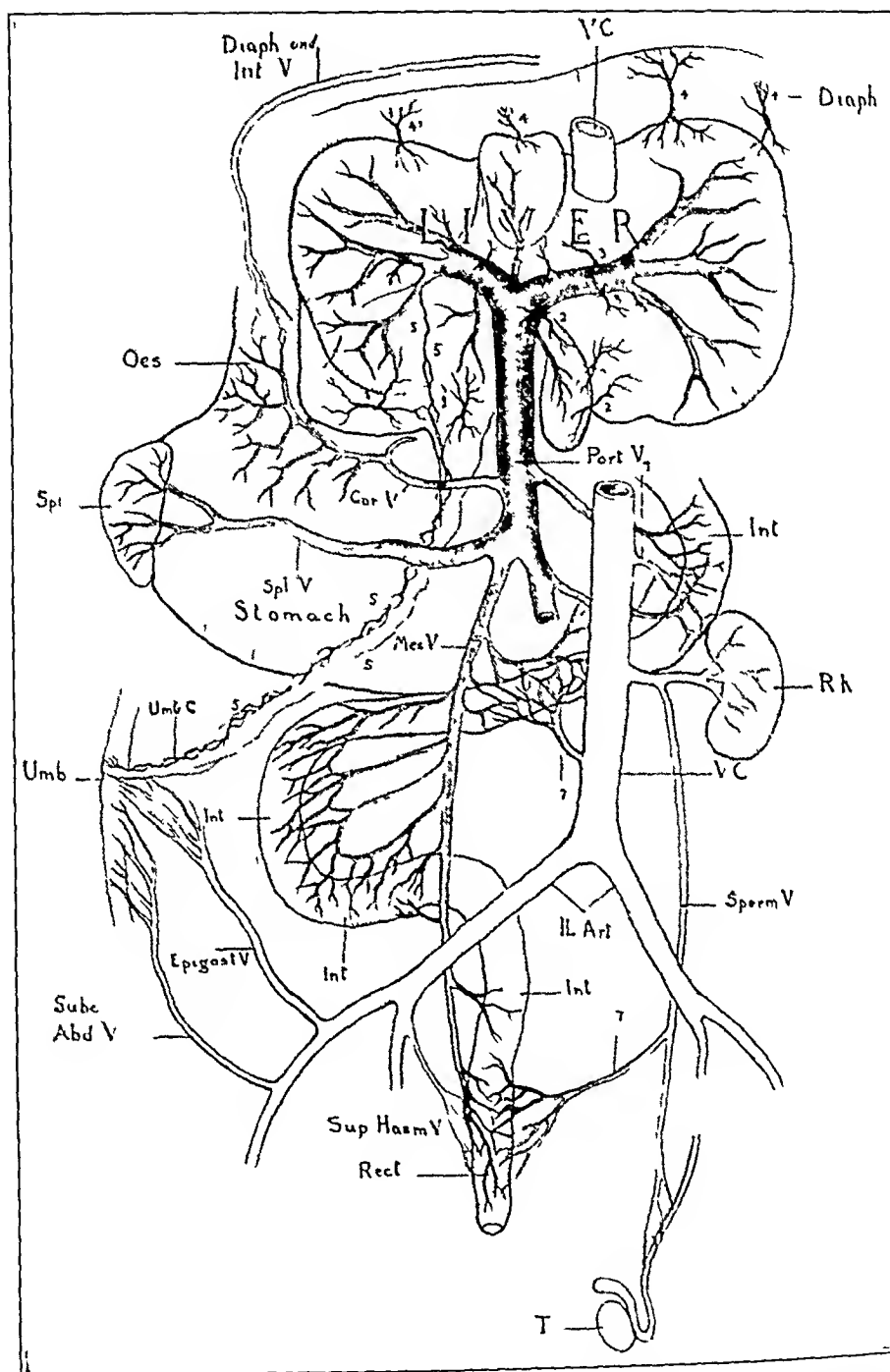


Fig 3—Diagrammatic representation of the collateral circulation established in portal cirrhosis of the liver. 1, 2, 3, 4 and 5 indicate the accessory portal veins of Sappey, 7 7 veins of Retzius posterior view. Abbreviations indicate structures as follows: *diaph*, diaphragm, *oes*, esophagus, *port v*, portal vein, *cor v*, coronary vein, *spl v*, splenic vein, *int*, intestine, *mes v*, mesenteric vein, *rh*, right kidney, *vc*, vena cava, *umb c*, umbilical cord, *sperm v*, spermatic vein, *epigast v*, epigastric vein, *sup haem v*, superior hemorrhoidal vein, *subc abd v*, subcutaneous abdominal vein, *il art*, iliac artery, *T*, testicle.

becomes easier." Cabot¹⁰ states that a correct diagnosis was made in 39 per cent of a series of eighty cases—certainly not a brilliant record—while in the same author's statistical review of 5 000 cases of ascites the following diseases appeared most common in the following order of frequency: cardiac, 1,397, renal, 665, cirrhosis, 325, tuberculous peritonitis, 263, ovarian and uterine tumors, 118, abdominal carcinoma, 109, intestinal obstruction, 86.

From these figures it would appear that approximately 7 per cent of all cases of ascites prove at autopsy to be due to portal cirrhosis. Simpson,¹¹ in discussing the diagnosis of portal cirrhosis, says that ascites is present in 50 per cent of all cases and in 85 per cent of the fatal ones, and that in 13 per cent of all cases in which the patients die of the disease, tuberculous peritonitis is present. When the ascites develops acutely, it is usually a terminal event. In the light of present evidence and the unfortunate lack of pathologic material obtained at operation, it seems justifiable to state that a positive diagnosis of portal cirrhosis can be made in the vast majority of cases only at autopsy. In addition to the conditions listed by Cabot, a differential diagnosis from Banti's disease must be made in the stage of cirrhosis and ascites. But Hopfner says that at this stage Banti's disease often cannot be differentiated from Laennec's cirrhosis, as in this condition also there may be splenomegaly and changes in the blood following cachexia.

TREATMENT

Hopfner, whose masterly review of the subject stands unique in the literature, classifies the possible methods of treatment as follows:

I Medical

II Surgical

1 Palliative—paracentesis

2 Radical

- (a) Omentopexy, splenopexy, obliteration of peritoneal cavity, etc.
- (b) Direct anastomosis between portal vein and veni cava.
- (c) Splenectomy.
- (d) Cardiolytic—extirpation of scar or new growth from liver.
- (e) Operation with unknown effect—exploratory operation for other purposes.

To this list might be added several methods of later development which involve attempted drainage of the peritoneal cavity either directly into the systemic venous circulation or into some part of the lymphatic system.

10 Cabot R. C. *The Causes of Ascites. A Statistical Review*. Boston, 1911. *Am. J. M. Sc.* **143** 1 1912.

11 Simpson A. I. *The Diagnosis of Peritoneal Disease*. Philadelphia, 1921. *Penn. M. J.* **25** 389 1921-1922.

I am not directly concerned with the medical treatment in portal cirrhosis. That cures have been thus effected is beside the point. Whether the fact that such cases become surgical only when despaired of medically militates against a possibly successful outcome from surgical intervention, it is difficult to say. On the other hand, the surgeon has accomplished little in the thirty or forty odd years of his endeavor to encourage the physician to transfer such cases. However, proper medical control, "when instituted in the formative stage of the disorder" (Osler), may prove effective. The general principles of this treatment involve such measures as rigid control of both food and drink, careful attention to both urinary and alimentary elimination, symptomatic handling of the various digestive disturbances and rational management of the various complications as they arise. Cures reported by the use of antisyphilitic therapy immediately take the case out of the class under discussion. The possibilities of drug therapy are limitless. For instance, Davis¹² reported the case of four patients treated medically with methenamine, elaterium, mild diet and rest, all of whom were cured, one remaining well after six years. He ingeniously remarks that the good results of surgical treatment are due to enforced rest during the surgical regimen. A patient of von Castaigne¹³ survived twenty-five years under medical treatment. Mercury and iodides seem to have some virtue, though here the possibility of specific action is again presented. More recently the synthetic compound merbaphen (novasurol) has gained some prominence in the treatment of patients who have ascites. Experience with this drug in one of my cases was not particularly favorable, after the second small dose the patient went into coma, and died within twenty-four hours. Autopsy revealed an advanced portal cirrhosis—a proved case.

Surgical treatment in this intractable disease has an ingeniously wide range. To warrant report of the numerous methods employed, some benefit in an occasional case must have been observed for each new operation. The variety of procedures indicates more clearly than anything else the unsatisfactory results obtained from any particular one. As a matter of surgical interest, the principal methods will be briefly described.

Hopfner's "palliative" surgical procedure, paracentesis abdominis, is undoubtedly the most widely used of all methods of treatment. It cannot, however, in any sense be regarded as a strictly surgical measure, for it is practiced with much greater frequency by the physician than by

12 Davis, N. S. Non-Surgical Treatment of Cirrhosis of the Liver, *J. A. M. A.* **61** 273 (July 26) 1913.

13 Von Castaigne, J. Sur un cas de cirrhose de Laennec avant évolue pendant 25 ans. *Bull. Soc. anat. de Paris* **72** 94, 1897.

the surgeon. Probably as many cures have been obtained by its employment as by any other single method. It is necessary to perform paracentesis on practically all patients postoperatively. According to Weber,¹⁴ cures following repeated paracentesis are "probably due to the formation of omental adhesions and gradual improvement of the collateral circulation." A mild peritonitis resulting from the repeated paracentesis doubtless plays an important rôle in these cures, as in Riesman's¹⁵ case. The patient, on whom paracentesis was performed thirty-six times for a total of 150 gallons, developed a fibrinous peritonitis after the last time, and was cured. Paracentesis was carried out in Drummond and Morison's¹⁶ famous first case forty-eight times before operation and sixty-one times subsequently. Examples could be multiplied indefinitely. There is apparently no limit to the number of times paracentesis can be carried out. Cases have been reported in which the patients survived 60, 111, 162, 298 and 303 tapplings. Such cases are certainly not the rule, for, as Hale White¹⁷ says, "The patient with ascites seldom survives many punctures."

The so-called radical surgical methods offer numberless variations. The history of the first reported cases is now familiar to every one. Though published in 1896, Drummond and Morison's case followed by several years Talma's¹⁸ first two cases in which the patients were operated on by Menlin in 1889 and by Schelky in 1891, respectively, though Talma did not report them until 1898. The general procedure of omentopexy is called the Talma-Morison operation. Variations of this procedure are as frequent as the operations performed. Probably two such operations have never been performed alike by the same surgeon. Schiassi¹⁹ has suggested an extension of the procedure. Incidentally, this author states that with his operation "the liver is examined carefully as are all other abdominal viscera and the existence of indications for operation are verified." This examination he regarded as "essential," and occasionally made further verification by histologic examination of tissue removed at operation. This statement, though made twenty-six years ago, stands almost unique in the literature, and is of course of fundamental importance. All the abdominal viscera have been trau-

14 Weber, F. P. *Hepatic Cirrhosis and the Question of the Operative Treatment of Chronic Ascites*. *Internat. Clin.* **1**: 88, 1924.

15 Riesman, D. *Spontaneous and Operative Cure of Cirrhosis of the Liver*. Report of Illustrative Cases, *J. A. M. A.* **76**: 288 (Jan. 29), 1921.

16 Drummond, D., and Morison, R. *A Case of Ascites Due to Cirrhosis of the Liver Cured by Operation*, *Brit. M. J.* **2**: 728, 1896.

17 White, W. H. *Cirrhosis of the Liver*, *Guy's Hosp. Gaz.* **12**: 205, 1898.

18 Talma, S. *Chirurgische Oeffnung neuer Seitenbahnen für das Blut des Vena Porta*, *Berl. klin. Wchenschr.* **35**: 833, 1898.

19 Schiassi, B. *La deviation chirurgicale du sang de la veine porte*. *Semaine med.*, 1901, p. 145.

matized more or less unmercifully and the diaphragm and the liver scrubbed with a coarse brush, the latter even painted with iodine, and occasional benefit has been noted. In all of these operative methods increase in the portal collateral bed is sought. That new channels are established is undoubtedly true, for, as W. J. Mayo²⁰ states, "The extent of collateral circulation established in this way is extraordinary. In several cases I made an incision mostly for other purposes, some time after omentopexy and encountered so much venous bleeding that I had to desist." In a case of mine in which the patient died three weeks after operation the portal circulation was injected, and definite collateral channels were found to be already established. Indeed, such vascularization is a familiar observation in ordinary omental adhesions when no portal obstruction exists—a fact of considerable significance in weighing the value of results obtained by omentopexy in cirrhosis with ascites.

Obliteration of the peritoneal cavity is usually accomplished more by accident than by design, and probably as frequently by repeated tapplings as by actual operation. If the procedure of draining a peritoneal cavity filled with ascitic fluid can have any justification, it is only on the basis of producing an intentional and inevitable peritonitis. Several cases are recorded in which ascites disappeared after a period of pyrexia and abdominal pain. Removal of a considerable portion of parietal peritoneum suggests itself as a possible means of accomplishing the same purpose. The operation of splenopexy, a rather formidable procedure, seems to have no possible rational basis.

Direct anastomosis between the portal vein and the inferior vena cava is by far the most alluring possibility of surgical treatment, but, though carried out successfully on animals in every experimental laboratory, few surgeons have had the temerity to apply it to human beings. One of the most interesting studies of the so-called Eck fistula from an experimental standpoint was that made by Hahn, Massen, Nencki and Pawlow²¹ in 1892. Of sixty animals, two-thirds died, while the remaining twenty were studied with the greatest care. These authors call attention to the similarity between the clinical picture which these animals presented and the terminal uremia exhibited in man in the presence of an advanced portal cirrhosis. The moment food was given, many animals developed symptoms of coma, and some died. It must be remembered that in the human being in whom cirrhosis has been gradually developing over a long period of time the few remaining liver cells

20 Mayo, W. J. The Surgical Treatment of Hepatic Cirrhosis, *Ann Surg* 80:419, 1924.

21 Hahn, M., Massen, V., Nencki, M., and Pawlow, J. La fistule d'Eck de la veine cave inferieure et de la veine porte et ses consequences pour l'organisme, *Arch d sc biol de St Petersburg* 1:401, 1892.

undoubtedly preserve the balance between actual life and death. Furthermore, it is likely that as the blood of the portal system is diverted by collateral circulation, whether spontaneously or as the result of surgical measures, the toxic symptoms which develop late in the disease may be due directly to this factor. Certainly ascites alone has never been the actual cause of death. As will be seen in the cases listed below, death followed operation in the great majority of instances after a comparatively brief time. Hahn and his co-workers believed that in the animals that survived an Eck fistula for a period of more than two weeks a collateral circulation probably developed through the liver, and these investigators felt that they had confirmed this observation by injections. Such a result in a person whose liver cells have already been largely replaced by scar tissue would seem highly improbable, although several authors surmise that after successful operative measures of any character the liver cells tend to regenerate. There is apparently no sound basis for such a contention. Furthermore, it is a well known fact that following the production of an Eck fistula many animals die of septicemia.

It seems, therefore, that though theoretically ideal for the relief of ascites, the diversion of all the portal blood directly into the systemic circulation in the presence of a cirrhotic liver is a procedure without proper, if indeed any, justification. Consideration of the technical difficulties of performing an Eck fistula on a human being is purely incidental in relation to the inevitably fatal outcome following its successful execution.

Splenectomy in portal cirrhosis is a method of treatment which has for its rationale only the obliteration of a considerable portion of the actual portal venous bed. Confusion in diagnosis is more evident in this group of cases than in any other. W. J. Mayo,²² for instance, speaks of ninety-seven patients on whom splenectomy was performed for splenic anemia, of whom forty-two "had more or less portal cirrhosis," while in nine cases of primary portal cirrhosis splenectomy and the Talma operation were performed, of the latter patients, two died in the hospital. Certainly few patients suffering from cirrhosis with ascites who present themselves for operation could withstand the rather extensive surgical measures necessary in splenectomy and omentopexy. The immediate postoperative mortality of the Talma-Morrison operation is slight. In only one of the cases of my series was splenectomy performed, and in that one the diagnosis was not absolutely clear.

Many cures have been reported following operations performed for some other purpose. Dr. Dean Lewis has described to me a case in

²² Mayo, W. J. The Surgical Treatment of the Cirrhoses of the Liver and Their Complications. *Ann Surg* 68:183, 1918.

which the patient was apparently cured by an operation for umbilical hernia, and Weber reports a similar instance. Frequent mention is made of cures in cases in which only an abdominal incision was made. There can be little justification for such conclusions unless the diagnosis has been confirmed beyond all peradventure.

Direct drainage of ascitic fluid into the blood stream by implantation of the saphenous vein in the peritoneum was described first by Ruotte²³ in 1907. This method is strictly designed to relieve a symptom, and in consequence is worthy of considerable attention, it is of additional interest in view of the fact that the large quantities of ascitic fluid with its contained protein are conserved for the patient. Repeated paracentesis necessarily results in a total loss of the material, and contributes to the patient's progressive loss of strength. Restoration of ascitic fluid by intravenous infusion has been practiced. Ruotte, Soyesima²⁴ and, most recently, Miller²⁵ have reported series of cases in which the patients have been treated by venoperitoneostomy. For relief of ascites the method seems to offer considerable promise, the only difficulty being the length of time during which the vein will remain patent. Urinary secretion is greatly increased, the fluid is drained satisfactorily, and, curiously enough, the heart is apparently unaffected by what must certainly be temporarily a greatly increased volume of blood. The operation itself is attended by a minimum amount of shock.

The more bizarre methods of surgical therapy, such as drainage of ascitic fluid directly into the bladder through a valvular opening in the fundus, suggested by Rosenstein,²⁶ the employment of silver tubes to effect permanent drainage into the subcutaneous tissues, and the utilization of the kidney pelvis and ureter as the drainage tract obviously involve a surgical risk out of all proportion to any likely benefit.

INDICATION FOR SURGICAL TREATMENT

The lack of accord between the physician and the surgeon as to the proper time for the institution of surgical intervention is undoubtedly the most serious obstacle to possible success. The failure of surgical treatment to show any uniform degree of benefit has developed a more or less natural hesitancy on the part of the internists to subject their patients to operation. There can be little doubt, however, that the

23 Ruotte. Abouchement de la veine saphene externe au peritone pour resorber les epanchement sciatiques, *Lyon med* 109 574, 1907.

24 Soyesima, von Y. Beitrag zur operativen Behandlung des Ascites bei Lebercirrhose, *Deutsche Ztschr f Chir* 98 390, 1909.

25 Miller, R. T. The Surgical Treatment of Ascites. Direct Drainage of the Fluid into the Blood Stream by Implantation of the Saphenous Vein in the Peritoneum. Report of Five Cases, *Penn M J* 19 413 (March) 1916.

26 Rosenstein P. Ventilbildung an der Harnblase zur Ableitung der Ascites flussigkeit, *Zentralbl f Chir* 41 373, 1914.

patients with portal cirrhosis and ascites are brought to the surgeon at a stage in the disease when little can be expected from any method of treatment. Furthermore, the uncertainty of both medical and surgical diagnosis adds greatly to this general confusion. If operation should be resorted to early, what is the proper time for such intervention? Practically all surgeons agree that surgical treatment should be instituted early and not as a last resort. Theoretically, the establishment of collaterals before ascites develops would be the ideal method of treatment. If there is any justification for surgical measures, the operation should be performed immediately after the ascites appears and not after repeated tapplings have debilitated the patient to an extreme degree and failed to afford any permanent relief. Might not prompt exploratory operation, in the absence of a clear indication of cardiac or renal disease, offer these patients with ascites a greater chance of benefit? Time lost in arriving at a 35 per cent correct diagnosis, though of academic importance, can add little to the patient's span of life.

Weber classifies the cases from a surgical standpoint in two groups.

Group A. Patients who for some reason—for instance, the presence of old perihepatitis and perisplenitis and extensive spontaneous omental adhesions—have a well established collateral venous circulation and do not readily develop ascites, but are of course liable to hematemesis from dilated esophageal or gastric veins. The liver is generally decidedly enlarged in this group of cases. Group B. Patients with a poor collateral venous circulation who develop ascites early. Weber maintains that the object of omentopexy and peritoneal drainage should be to convert group B patients into group A patients. Obviously, the sooner the collaterals are established the better the effect should be.

The results of surgical treatment as reported in the literature are extremely difficult to analyze. From general compilations of reports of cases and series, it seems that cures and marked improvement may be expected from all methods in from 35 to 50 per cent of the cases. No figures or data are available as to the optimum time in the course of the disease for surgical treatment or the actual type of operation offering the greatest chance of relief. Some form of omentopexy is the operation of usual choice, so that to it must be given the greater part of whatever credit belongs to surgical treatment. Few series have been reported, however small, in which some apparent benefit has not resulted from operation. Combined treatment, medical and surgical, may produce benefit when the surgeon or internist alone can accomplish little. Certain it is that the disease is one which at the present time can have only one outcome under strictly medical control. If in an established case operation can offer any hope of benefit—and apparently it can—the surgeon should see the patient early and determine the moment best suited for operation.

PRESENT SERIES

In the study of the present series great difficulty has been encountered in selecting from the rather considerable group of cases listed portal cirrhosis with ascites those which belonged definitely to this group. At first about fifty cases were selected. After critical examination of the history and analysis of the operative observations, twenty-six cases were chosen as representing more or less accurately the disease, portal cirrhosis (table of cases). In the earlier cases a careful operative note as to the condition of the liver, the degree of dilatation of the portal tributaries and the apparent thickening of the peritoneum, together with negative observations as to tuberculosis, carcinoma and other diseases, had to serve as the basis of selection. Autopsy records offered conclusive proof in a small number of cases, and in the more recent ones a section of the liver removed at operation furnished the necessary evidence. Two of the cases that I list still seem doubtful, but they have been included on a more or less reasonable basis. It will be seen, therefore, that in a group of fifty cases diagnosed clinically as cirrhosis of the liver, confirmed to some degree at operation and subjected to a properly critical analysis, only 50 per cent can be placed with accuracy in this group. These patients have been operated on over a period of about thirty years by a succession of surgeons representing, of course, varying degrees of skill and judgment. There is only one considerable series of patients operated on by a single surgeon, it includes twelve of the total number of cases. In this particular group a variety of operations was performed, but each involved laparotomy with some additional measures. Few of the earlier cases were followed, and the last clinical note has of necessity been taken as the probable duration of life, the later cases indicate that these figures probably are accurate.

Though statistics are of no particular significance, this series seems of sufficient size to warrant tabulation of certain facts evolved from a study of the cases. Comparison with other reported series has been purposely avoided, as I believe no group of similar size has previously been compiled on the basis of the standards outlined above.

Twenty-six patients are represented, of these twenty-two were males and four females, twenty white and six colored. The average age was 42 years, the youngest, $4\frac{1}{2}$ years, and the oldest, 66 years. The decades were represented as follows: first, 1 case, second, 2 cases, third, 1 case, fourth, 3 cases, fifth, 9 cases, sixth, 8 cases, and seventh, 2 cases. More than half of the cases, therefore, occurred in the fifth and sixth decades.

Discrepancies between the subsequent data and the total number of cases are accounted for by lack of data in the clinical records. The

average duration of symptoms of all kinds before operation is eight months, the shortest twelve days and the longest two years. The onset was characterized by acute abdominal pain in eight cases, abdominal swelling in thirteen and hemorrhage in three. Fifteen of these patients gave a definite history of potatorium, five had syphilis. In the patients on whom paracentesis was performed before operation this procedure had been carried out for an average of four times and an average amount of seven liters of fluid had been obtained. Dilated superficial abdominal veins were noted in five cases. The following operations were performed, more than a single procedure was carried out at one time in some instances: simple laparotomy, 3, peritoneum and liver scrubbed, 9, omentopexy (all varieties), 12, cholecystostomy, 2, splenectomy, 1, liver painted with iodine, 1.

Reaccumulation of fluid is recorded in seventeen cases, in all of which paracentesis was performed from one to eight times postoperatively. Three patients were treated by drainage. One patient (case 23) was alive and in good health three and one-half years after operation. This case will be referred to later, as it is the only one in the group of twenty-six in which the clinical diagnosis alone was accepted as final. When last heard from, one patient, the first, was alive eight months after operation, two patients were alive four months, two, two months and four, one month after operation. These patients subsequently failed to answer letters of inquiry. Sixteen of the twenty-six patients are known to be dead, having survived operation for an average of twenty-two days, six of this number died within one week, four survived a month, one two months and one approximately three months. All types of anesthesia were used.

An analysis of the data in the preceding paragraph and some further specific observations fail to support any of the favorable conclusions arrived at in other reported series. In this group of cases particular emphasis has been laid on the operative confirmation of clinical diagnosis. In three instances such evidence was not available from the records. In the first case, in which operation was performed on Nov. 6, 1896, the history and the notes of the physical examination were classic descriptions of portal cirrhosis with ascites. The operation of "median laparotomy" was performed simply to liberate the ascitic fluid, no mention being made of the condition of the liver. A note made in June, 1897, states that there was no fluid in the abdomen and no edema of the legs, and that the patient had resumed a thirty year custom of drinking heavily.

The youngest patient in the group (case 19), on whom a splenectomy was performed, died four days after operation. This case does not belong strictly to the portal cirrhosis group as the pathologic picture was

Compilation of Twenty-Six Cases of Portal Cirrhosis with Ascites

No	Sex	Race	Age	Duration	Times Tapped	Average Amount	a Potatorum b Syphilis	Type of Onset	Comments on History	Operation	Postoperative Course	Course After Operation	Comments
1	M	W	50	12 days	—	—	a ++++ b —	Acute abdominal pain	On spree for three days	Laparotomy 11/6/96, release of fluid	Two weeks later slight reaccumulation	Well 8 mo	Started drinking again
2	M	O	41	1 mo	—	—	a — b —	Acute		I 2/8/97 peritoneum scrubbed, II 3/6/97 laparotomy, 9 liters	3/3/97 marked reaccumulation, 4/2/97 reaccumulated, 1/19 6 liters	Alive May 1	Transferred to medical service, liver enlarged, peritoneum thick
3	M	O	37	2 yr	+	3 liters	a ++++ b +	Attacks of dyspnea	Medical treatment successful, large veins	2/10/97 liver and peritoneum scrubbed	Tapped twice no relief	4/12/97, discharged	Became hysterical
4	M	W	44	—	—	—	—	—	—	9/16/97 liver and peritoneum scrubbed, 2 liters	Pleural peritoneum, fluid three times 7/6, 8 liters	10/22/25 transferred	Large hobnail liver, peritoneum thick
5	M	O	40	5 mo	1	9 liters	a + b —	Swelling in legs and abdomen		8/20/00 6 liters liver, glands, peritoneum scrubbed	Great shock	8/23/00 dead	Hobnail liver, thick peritoneum
6	M	W	51	1 mo	+	13 liters	a + 1 + +	Gradual swelling		4/25/02 liver and peritoneum scrubbed, omentum adhered to abdominal wall	5/19/02, tapped, 9 liters	5/30/02, died in coma	Hobnail liver, thick peritoneum, large veins
7	M	W	42	9 wk	+	3 1/2 liters	a +	Nausea and vomiting		5/8/02 liver and peritoneum scrubbed, drained		5/11/02 dead	Hobnail liver, thick peritoneum, stupor
8	F	W	55	1 mo	1	5 7 liters	a +	Hemorrhage, pain, vomiting, swelling	Large veins over abdominal dome	10/5/02 liver scrubbed, rubber drainage tube inserted		10/7/02 dead	Cirrhotic liver, veins greatly dilated
9	M	W	43	2 mo	+	6 liters	—	Hemorrhage and swelling		3/20/03 liver, parietal and visceral peritoneum scrubbed with gauze, omentum to abdominal wall	4/6/03 tapped, 4/16 8 liters 1/23 7 liters	4/26/03 dead	Hobnail liver, thick peritoneum
10	M	W	55	1 mo	+	5 liters	a ++	Pain over liver	Jaundice for 1 year, slight	3/15/07 peritoneum scrubbed	3/20 4 liters	3/23 dead	Liver cirrhotic, gallbladder thickened, fluid rather milky
11	M	W	62	6 mo	—	—	a ++	Abdominal pain, no swelling	Slight jaundice	10/28/08 cholecystostomy	6/ 5 8 liters	12/9/08 improved	Cirrhotic liver, contracted gall bladder, liver small and cirrhotic
12	M	O	22	2 1/2 yr	—	—	a ++++	Swelling only	More rapid swelling in months before operation	5/23/10 laparotomy 18 liters	6/11 8 liters 6/18 5 liters 6/23 6 liters 7/1 5 liters 7/7 4 liters	Improved 9/3/10 fluid forming much more slowly	Abdomen simply explored

13	M	W	40	1½ yr	+	13	?	a + + + + + b + + + + +	Swelling of feet and ankles, hemorrhage 6 mo before Dr Hughson was consulted	Prominent veins	2/20/11 omentopexy (Schrassi) 10 liters	2/25 2 liters (pleura) 2/28 7 liters 3/1 8 7 liters 3/12 7 liters 3/24 7 liters 9/26 7 liters	5/8 ascites still present, pt ill, 5/12 died in coma	Liver cirrhotic, omental veins dilated
14	M	W	55	10 mo	+	3	20 liters 12 liters 10 liters 5 liters 5 liters	—	Jandice	—	9/6/16 omentopexy, 10 liters	—	Increase slow, 10/2/16 improved	Liver large and hobnail
15	M	W	41	2 mo	+	3	10 liters 5 liters 5 liters	—	Abdominal pain, vomiting	—	9/14/21 Talm operation on liver and peritoneum scrubbed	—	No recurrence of ascites, 10/13 discharged inproved	Liver not typical hobnail, described as dark red with irregular surface, adhesions present
16	M	W	43	1½ mo	+	12	5-8 liters	a + + + + + b + + + + +	Abdominal pain vomiting	Acute nephritis, jaundice, ascites returned	3/6/24 omentopexy, large amount of fluid 10 liters	3/11 8 liters 3/11 other times average 7 liters 2/18/25 2 liters	3/25/24 hobnail liver, no relief, death	Marked cirrhosis
17	M	W	38	1 mo	+	3	4 liters 4 liters	—	Jaundice, chills and liver	Ascites came on later	2/9/25 omentopexy, liver and peritoneum scrubbed 4 liters	—	2/23/25 Cirrhotic liver, everything else thought normal	Marked cirrhosis
18	M	W	48	1 yr	+	5	?	Three glasses of beer per ankle and day for 7 yr	Swelling of ankle and abdomen	—	6/25/25 Schrassi omentopexy	8/1/25 dead	3/9/25 dead	Hobnail liver, thick peritoneum death followed by merbaphen (novasurol), autopsy spleen slightly enlarged
19	M	W	4½	—	—	—	—	—	Weekly swelling of abdomen, fluid	Collateral cirrhosis marked	7/17/24 1 liter splenectomy	—	7/21/24 dead	Cirrhotic liver, dilated veins, peritoneum thick
20	M	W	31	1 mo	Op 2 mo ago	1	5 liters	a + + + + + b + + + + +	Heavy feeling in stomach	No response to antisyphilitic treatment	10/25/23 omentopexy, 3 liters	11/1 5 liters 11/7 6 liters	11/8/23 discharged to Bay View	Cirrhotic liver, dilated veins, peritoneum thick
21	M	W	51	19 mo	+	1	6-7 liters	a + + + + +	Vomiting, swollen stomach	Liver function test points to iodine	3/3/24 omentopexy, liver punctured with iodine	3/6 7 liters	4/23/24, dead	Hobnail liver, cirrhosis
22	M	W	49	1 mo	+	8	?	?	Swelling	Large veins cirrhosis	8/8/23 omentopexy	—	8/8/23 dead, hemorrhage	Cirrhotic liver, huge omental veins, autopsy
23	M	W	46	—	—	—	—	—	Clinical diagnosis of ascites and cirrhosis	—	12/22/00 cholecystostomy	—	10/21/01 well, no difficulty, gained 20 lbs (9 Kg), 5/2/03 good health	No exploration of liver at operation
24	F	O	16	2 yr	1	3	Large amount	—	4/22/06 medical service with C.B. neg large liver	Fluid and large liver	8/1/07 suture of liver and omentum to parietal peritoneum	—	8/30/07 excellent condition	Before operation fluid had disappeared, liver soft and mottled, adhesion between liver and parietal wall
25	F	W	31	1½ yr	—	—	—	W isserum reaction negative	swelling, dyspnea and spleen	No fluid	11/17/16 exploratory laparotomy, fluid 1/23/17 cholecystectomy	—	11/20/16 dead, coma	Liver hard rough and contracted, cirrhotic
26	M	W	50	2 yr	—	—	—	Slight drinking	Fulness in flanks	Liver and spleen large and firm	—	—	5/23/17 much improved, no fluid	Liver enlarged and cirrhotic, also spleen, stones in gall bladder

much more that of Banti's disease. In case 18 a positive clinical diagnosis of portal cirrhosis with ascites was made at operation on Dec 22, 1900. Exploration was not made of the liver, or at least no observations were noted in the history, but stones were found in the gallbladder, and a cholecystostomy was performed. Three and one-half years after operation this patient was alive and well, having gained 20 pounds (9 Kg). This represents the longest known period of survival in this group of cases, and occurred in a patient presenting ascites and a clinical diagnosis of portal cirrhosis without operative confirmation. It seems reasonable to regard this as an unproved case and consequently of little value in relation to end-results.

There are, therefore, two unproved cases representing the longest periods of survival following operation, eight months and three and one-half years, respectively, in which operations were performed without reference to any idea of establishing collateral circulation. And these are the only cases in the series of twenty-six which can be regarded as offering any justification for surgical treatment in portal cirrhosis with ascites. The first patient was operated on two months after the publication of the article by Drummond and Morrison, and the operator was no doubt unfamiliar with the procedure of omentopexy.

Of the remaining patients, a simple laparotomy was performed on one (case 12), and his abdomen was tapped six times after operation, five months later he was considered improved, since fluid was forming much more slowly. This patient was then lost to observation, so far as further records are concerned. The patients in cases 2, 3, 4, 14, 15 and 26 were followed for a brief period and also lost. The patient in case 26 showed jaundice, the only one in the group, and he was possibly ineligible on that account. It has been an almost invariable experience that patients with atrophic portal cirrhosis do not have jaundice. This patient had a cholecystectomy performed, and at the end of one month was considered improved. The remaining seventeen patients, or 65 per cent of the total number, not only did not show improvement, but they died on an average of three weeks after operation. In each of these cases there was operative confirmation of a clinical diagnosis, in several the additional support of autopsy observations was available. In other words, the only patients in whom there was no reasonable doubt as to the diagnosis and who could be followed for a sufficient length of time died within an average of three weeks after operation. In every instance the operative measures were designed to increase the collateral circulation of the portal system.

In these twenty-six cases a relation between the general postoperative course, the total period of survival or the temporary degree of improvement and the duration of the disease before operation is not apparent.

Frequent preoperative tapplings were not associated with improvement any more than with fatality, nor did the particular decade seem to influence the general course

COMMENT

The difficulty of reconciling the facts outlined in the foregoing study with the numerous reports in the literature is apparent. Observers of unquestioned accuracy and authority list in their series of published cases instances of definite cure. Weber, for instance, reports a patient alive eight and one-half years after operation. In an article on the surgical treatment of hepatic cirrhosis, W. J. Mayo reports forty-seven operative cases with seven deaths in the hospital, twenty-one patients alive when last heard from, and four patients well at nine, eight, seven and five years, respectively. The differentiation of cases in this series is not clear, as the splenic anemias are all described as being associated with "more or less portal cirrhosis." The same author states that the "Talma-Morison operation per se carries only a slight risk." Riesman reports three interesting cases resulting in cure, one after thirty-six tapplings and the development of a fibinous peritonitis, and the other two following omentopexy. He further says "I have seen the Talma operation fail, owing I believe to my having postponed it too long," and he also believes that "cure of its outstanding symptom, namely the ascites, brings about arrest or cure of the cirrhotic process the damage done to the liver seems to be compensated." Judd and Lyons²⁷ say that in the presence of jaundice and a large amount of ascites the Talma-Morison operation has not been satisfactory, while in cases in which there is no jaundice and in which the quantity of ascites is not too great or the liver too badly diseased, this plan of transferring the circulation has seemed to accomplish a great deal. This is a reasonable statement of fact, it seems, for in the first group there would be no indication for the operation and in the second there would surely be doubt of existent disease. King²⁸ reports an interesting case of a woman who was operated on when bedridden and delirious, paracentesis was performed fifteen times after operation, and four years later she was apparently cured. In 1918, W. J. Mayo reported five of twenty-eight patients treated by the Talma operation as cured. Hale White's collected series is most striking. Of the hypertrophic variety twenty-four cases are listed with ten patients cured, six improved, three unim-

27 Judd, E. S., and Lyons, J. H. The Mortality Following Operations on the Liver, Pancreas and Biliary Passages, a Statistical Study, *Ann Surg* 78 194, 1923

28 King, E. L. Presentation of a Case of Cirrhosis of the Liver. Talma Operation. Entire Relief from Symptoms, *New Orleans M & S J* 20 72 520 1919

proved and five dead. Of the atrophic group of sixty-two cases, thirty-eight were cured, seven improved, seven unimproved and twenty-seven dead.

Eliot and Colp²⁹ summarize their observations by saying that the most favorable cases occur between the second and fourth decades in fairly well nourished persons without severe nephritis, cardiac lesions or compensatory circulation, with a hypertrophic liver, on whom paracentesis has been performed a few times, and in whom disease comes on slowly for one year or more. "That the operation under local anesthesia is a benefit in carefully selected cases," they say, "there can be no doubt." These qualifications seem difficult of fulfillment. In the series herewith reported only six of the total number of twenty-six cases developed in persons between the second and fourth decades, the average preoperative period was eight months as against an optimum of a year or more, superficial collateral circulation appeared in a comparatively small number of patients, and on the majority paracentesis was performed one or more times prior to operation. As has already been noted, no significant difference could be recognized in the general post-operative course of any of these patients. Such data can be multiplied indefinitely from reports of series and isolated cases, but the purpose of the present discussion is not to compile the reported cases.

SUMMARY

The problem under discussion must be regarded from several angles. In the first place, the disease is comparatively rare, and offers many difficulties from the standpoint of differential diagnosis. Cabot states that a correct diagnosis was made in 39 per cent of eighty cases. From our own observation this proportion seems too high. The only positive method of diagnosis is by section at operation or by autopsy. Hemorrhage and ascites are inconclusive. Hepatic enlargement is referred to frequently as a favorable circumstance, and yet a large liver is present in many conditions which cannot possibly be regarded as true portal cirrhosis. Of my last three patients suffering from "portal cirrhosis with ascites," at operation one was found to have syphilis, another tuberculosis and the third Banti's disease with secondary enlargement of the liver.

The surgical treatment of portal cirrhosis with ascites, except for the methods designed to institute direct drainage, is a random sort of procedure. On the basis of an omentopexy of some type to stimulate an extensive collateral circulation, every imaginable method has been employed. As indicated in the present series, the liver and the intestines

²⁹ Eliot, E., and Colp, R. The Operation of Omentopexy in Cirrhosis of the Liver, *Surg Gynec Obst* 28:309, 1919.

have been scrubbed and the liver has even been painted with iodine, in every instance death has ensued with varying degrees of promptness. Drainage and nondrainage have their advocates, the objection here as elsewhere being directed against the likelihood of infection of a previously sterile effusion. And yet one frequently encounters in the literature the significant observation that an apparently mild peritonitis with its associated pain and fever was followed by an apparent cessation of the production of ascites. This peritonitis has followed both surgical treatment and what may be called medical drainage, or paracentesis.

A brief digression may be made here to emphasize again the almost uniform observation of a thickened peritoneum. Simpson draws attention to this fact, and states that most cases show a chronic peritonitis. It is probably safe to go further and say that all cases of any particular duration exhibit a chronic peritonitis. The peritoneum normally absorbs fluids rapidly. The thickened peritoneum of a portal cirrhosis could not possibly absorb, and undoubtedly plays a fairly important part in elaborating the fluid. Might it not be reasonable, therefore, to explain possible benefit obtained from surgical intervention on the basis of obliteration of the peritoneal cavity from whatever cause rather than from the establishment of a doubtfully adequate collateral circulation? As a possible form of treatment, removal of large areas of parietal peritoneum suggests itself for the surgical obliteration of the peritoneal cavity without having recourse to infection.

Late improvement following surgical treatment has been explained on the basis of a regeneration of liver cells following the relief of the portal circulation. There is, of course, no evidence to support such an assumption, and again the difficulty of correct diagnosis must serve to temper enthusiasm in analyzing favorable results.

CONCLUSION

In the present series of twenty-six cases regarded as correctly diagnosed from either operative or autopsy observations or both, it is impossible to conclude that surgical treatment instituted for the purpose of establishing additional collaterals is of the slightest benefit in portal cirrhosis with ascites.

Furthermore, from a study of this series no evidence can be adduced which would indicate that any particular age, sex, race, period of disease or time of appearance of ascites is more favorable for the employment of surgical measures than any other. It seems true, however, that in the great majority of cases operation was performed as a last resort, this statement is made without reference to the possible advantage of surgical intervention.

The difficulty of accurate diagnosis must be borne in mind in reporting favorable surgical results. None but proved cases should be listed.

On the basis of correct diagnosis, which is estimated at 40 per cent, the figure generally accepted as representing the expected benefit from operation, 35 per cent, would fall to approximately 10 per cent, and more careful analysis would undoubtedly reduce the estimate even further. An additional source of error lies in the loose application of the term cirrhosis, omentopexy and its subsequent variations and elaborations were designed for the treatment of portal cirrhosis with ascites.

Though the fact possibly has no significance so far as the etiology of the disease is concerned, it is noteworthy that 60 per cent of the patients in the present series gave a definite history of potatorium.

INVAGINATION ILEUS IN POLYPOSIS OF SMALL INTESTINE*

REXWALD BROWN, M D

SANTA BARBARA, CALIF

REPORT OF CASE

S B, a girl, aged 21 months, was sent to the Santa Barbara Cottage Hospital on June 7, 1926, by Dr E J Lamb, who had made a diagnosis of intussusception. I saw the child, concurred in the diagnosis and opened the abdomen at once, twelve hours after the onset of symptoms. An intussusception was found in the small intestine about 1 foot (30.4 cm) above the ileocecal juncture. The invagination was reduced by manipulation. When normal continuity of the bowel was restored, complete obstruction by a solid mass was found in that portion of the intestine which had been the intussusceptum. A portion of intestine, 3 inches (7.6 cm) long, which contained the mass, was resected, and a lateral anastomosis was performed. The child made an excellent recovery and is now in good health.

The pathologist of the hospital, Dr F R Nuzum, reported that the tumor was a benign intestinal polyp with a broad base.

REVIEW OF THE LITERATURE

Beginning with R C Coffey's comprehensive paper on intussusception, which appeared in 1907, I have made a considerable survey of the literature on intussusception. Since Coffey's paper, in which he reported a mortality of from 70 to 90 per cent, the range of mortality in the services of various physicians who have handled this condition or reviewed a series of cases from several clinics has been from 25 to 65 per cent. There is one record of stellar prominence, however, in the management of intussusception, that of Hipsley of Australia, who operated on fifty-one patients, without a single death. This outstanding achievement is a challenge to American physicians to better understanding of intussusception, an anatomic tragedy which, though not rare is by no means of common occurrence in the routine practice of internists, pediatricians and surgeons. Hipsley's success was due to accuracy of diagnosis, dependent on symptoms as classic as those of acute appendicitis, and to immediate operation following diagnosis. All of the fifty-one patients were treated surgically within thirty-six hours after the onset of the condition. Deaths occurred in Hipsley's service when operation was not performed until thirty-six hours had passed since the onset of intussusception.

The high mortality in America is due first to failure of physicians to appreciate the significance of intermittent screaming and crying,

* Read before the Pacific Coast Surgical Association Feb 25 1927

vomiting, apparent abdominal pain and bloody mucoid stools manifested by an infant that previously has been well and happy, and, second, to procrastination or unwise treatment when the diagnosis of intussusception has been made or suspected

The clinical history outlined in my case portrays two aspects of intussusception concerning which, because of their infrequency, a voluminous literature does not exist. One aspect is that the ileus was caused by a polyp or, more accurately, by a polypoid tumor within the intussusceptum of the ileum, the other, that the recovery of an infant after resection for invagination ileus is a surgical curiosity

Polypoid formation in the small intestine is apparently so rare that clinicians give slight consideration to the condition, and textbooks on pathology mention it only in passing. This is in contrast to a rapidly increasing literature detailing adenomatous polypi, occasionally single and frequently multiple, in the rectum, large intestine and stomach. According to some clinicians, invagination ileus plays the principal part in the symptomatology of polypoid formation, whatever the location of the polypi, whether the growths are single or multiple, and independent of the age of the patient

These clinicians suggest an etiologic basis as follows: "The bowel below the tumor block atrophies and stretches and the bowel above incident to peristaltic movements slides on into the gaping segments." Nevertheless, it must be acknowledged that, with or without formation of a tumor, a verified explanation of the *modus operandi* of intussusception has not yet been given

That invagination ileus is a dominating feature in the symptomatology of polypoid growths is not borne out by a series of cases of gastro-intestinal polyposis reported by Struthers, of the Mayo Clinic, in 1923. There was not one case of intussusception in his series

Recovery after resection in intussusception in an infant or young child is seldom chronicled. E. W. Peterson, in 1905, reported in the *Medical Record* what he believed to be the first successful resection for the relief of intussusception. The same author, in 1922, in *Surgery, Gynecology and Obstetrics*, stated that less than a score of successful resections in infants were on record. In the literature are such statements as the following: "In 429 cases of intussusception at St. Bartholemew's Hospital there were nine resections—all nine died," and "In studies of 400 cases by Massart there were eight resections done with eight deaths." I believe that the high mortality in resections is not due to the trauma of resection itself but is part of the appalling mortality incident to failure to recognize invagination ileus, or to late treatment for the condition

HUMAN FACTORS IN CLINIC MANAGEMENT

A STUDY MADE IN THE SURGICAL AND FRACTURE CLINICS
OF THE OUTPATIENT DEPARTMENT OF PRESBY-
TERIAN HOSPITAL

MARY K TAYLOR, A B, B S

UNDER THE DIRECTION OF JANET THORNTON, A B

MATERIAL COMPILED BY FLORENCE HARVEY

WITH A FOREWORD BY DAVID C BULL, M D

NEW YORK

FOREWORD

The study of the management of patients in minor surgical care made in the outpatient department of the Presbyterian Hospital with the cooperation of the Committee on Dispensary Development illustrates a valuable method for the investigation of the problems of clinic management. It presents, on a statistical basis, certain known faults considered of minor importance and more or less inevitable with the ever-changing staff of a teaching clinic. The frequency of their occurrence and the amount of harm that they cause had not been realized.

The study shows the degree of disorganization and delay due to teaching as practiced simultaneously with treatment. We have therefore increased the number of surgeons on duty and thus freed the instructor from responsibility for the treatment of patients during the period of teaching. At the same time it was discovered that it was unsafe to assign responsibility to interns, and they are now present for instruction only.

Social problems are shown to be caused or increased by minor surgical disabilities, and we have secured an additional social worker to meet these needs. We have come to a greater realization of the large social element in the handling of patients in the clinic, and feel that lay personnel should be selected on the basis of ability to understand and manage people, an ability which is best developed by training in social case-work methods.

This study throws some light on the moot question of the advisability of general physical examination of all patients. Some of the patients interviewed in this study would have welcomed inquiry into conditions other than the definite surgical complaint—there was something distinctly on their minds—anxiety concerning blood pressure, arthritis or some other question brought up by the propaganda for periodic health examination. We expect that these patients may more readily be singled out with provision of greater privacy and opportunity for concentration.

on the person. As an experiment in this direction we have introduced individual treatment cubicles into the plans for the surgical dressing rooms of the new Medical Center.

We realize that this study is one-sided in that it emphasizes only the pitfalls that beset clinic practice. We feel that an analysis of the favorable elements on which success depends in the properly handled cases would be as illuminating and instructive.

It is because we suspect that the faults occurring in certain of our clinics may be duplicated in other institutions that we are glad to have this study published. It presents a mechanism for collecting data on the basis of which existing faults may be detected and technics of clinic management built up.

AIM AND METHOD OF STUDY

Physicians have always recognized the need of understanding not only the pathologic processes of organs and tissues, but also the patient in his aspect as a person. As the practice of medicine has grown more complex, greater cooperation on the part of the patient has become necessary, and at the same time, psychologic methods have been developed to study his personality and to influence his behavior. Meanwhile, there has been an enormous increase in the number of persons applying for outpatient care and in the cost of such care, while modern ideals of medical practice demand more individualized attention for each patient.

The strain the increased number of patients has placed on existing procedures and forms of management has brought to light inadequacies and defects not previously apparent. Thus the problems confronting the administrator of a modern outpatient department have become greater and more varied than ever before. Many of these problems are similar to those of business organizations handling masses of people and endeavoring to give satisfaction to each person. In an effort to meet the situation, business organizations are testing their efficiency by "job analysis" and the formulation of technics—a movement to which impetus was given by the necessity of wartime.

The Committee on Dispensary Development recognized the need for similar tests and study in connection with the administration of medical care in outpatient departments and undertook to make careful observation of the best existing practices and the results achieved in the management of patients.

Aim—In an effort to arrive at a method by which efficiency in the management of patients could be tested and results evaluated, the question naturally arose, "For what purpose is the clinic run?" If it is assumed that the answer must be, "To give adequate medical care to patients," the next question is "How do we know whether adequate

care has been rendered? How are we to find out? What conditions make for adequate care?" Except for the reports of visits made, revenue received, cost of care and other items and the study of end-results in the comparatively few cases in which research has been of interest, there is no method of testing and evaluating the service of the clinic as a whole. It is for this reason that physicians engaged in the actual treatment often struggle to care for far more patients than they can treat adequately. They are often supported by assistants chosen because of their willingness to work for low pay and entirely unequipped to manage patients in a clinic. Administrators have been concerned with keeping down the cost of service, and have been unaware that service has not been rendered.

A method of testing and evaluating management of patients was devised, and a study was made by members of the staff of the Committee on Dispensary Development, in 1925, in the outpatient department of the Presbyterian Hospital in New York, with the approval of Dr. Allen O. Whipple, director of surgery, and in collaboration with Dr. David C. Bull, chief of the surgical clinic. A clinic dealing with minor surgical treatment was selected with the idea that the problems of management were simple compared with those of a more complicated general medical clinic previously studied.¹ As will appear, the observations indicated that even in these minor surgical clinics, what may be called the management quotient was high.

Scope—In making the study, emphasis was placed, not on the management of *disease* nor on the diagnosis and therapy for different conditions, but on the *management of patients*, and on the staff and plant required to serve them. The experience of a number of unselected patients was analyzed. These cases were studied with a view to obtaining a picture of each patient in his social and economic setting and in relation to his disability at the time of his admission to the surgical clinic, throughout the course of treatment, and at the time treatment was discontinued. It was proposed that the study of each case, with interpretation and assistance by the physician throughout the course of treatment, should bring out the patient's disability in terms of discomfort and inability to carry on his usual occupation, a forecast (on date of diagnosis) concerning the outcome expected and the amount of time necessary for treatment and recovery, the plan of treatment, the elements of difficulty and expense entering into the giving of treatment and the giving and carrying out of advice and a description of the rôle played by the surgical and adjunct services and by the patient and other agencies outside the hospital.

¹ Bradbury, Samuel M. D. What Constitutes Adequate Medical Service? New York, Committee on Dispensary Development, December, 1926.

It was not possible to carry out this plan entirely, as the physician did not have the time to give the forecast in each case. It also proved impossible to obtain information from all patients as to the cost of their disability in terms of time lost from work.

Method—One hundred and fifty-five cases—about a tenth of all new cases admitted to surgical and fracture clinics—were studied between January 8 and May 31, 1925. Thirty-five (22.5 per cent) of the patients had had their first treatment for the present disability in the emergency ward. Not all the patients were studied to the end of their treatment, since seventeen were still active when the study was terminated. It was not possible to study all new cases, since the worker was occupied part of the time in observing treatment.

The method of collecting the information was as follows:

The study worker interviewed each new patient on the waiting bench before he was admitted to the clinic for treatment. To afford a natural approach, the worker took the initial history of the disability, unless, of course, the patient had been previously treated in the emergency ward for the same complaint. The history was written directly on the medical record for the physician's use. It consisted of the standard items—chief complaint, duration, present history and past history when indicated. In addition to the history of the present illness, the study worker recorded the occupation and process, wage, composition of the family and its income, time lost from work for present disability and the effect of this disability on the patient's daily life and work. She also tried to get a picture of the general situation of the family with a view to learning of any existing social or health problems.

The worker then accompanied the patient into the clinic and observed and recorded, as far as possible, the treatment and instructions that were given to him, such as operations, dressings, advice and time of return appointment. When he left the clinic, the worker interviewed him again, asked him what advice he had received and whether he understood it, and noted the time of his departure. He was also asked how much time he had to spend en route, what time he had arrived at the clinic and what expense he had for transportation and treatment. This process was repeated on each subsequent visit, and in addition to these questions the patient was asked his opinion of his progress, what difficulties he had experienced in carrying out his instructions and what difficulties had resulted from his disability. All these facts were recorded each time on study sheets kept on each case. In many instances the worker found that the patient did not understand his instructions or wished to ask questions which he had been unable to ask in the clinic. In each of these cases he was referred to the proper person to adjust the difficulty. According to the study worker, the difficulties recorded

are approximately typical in variety and number of those occurring in ordinary practice in these clinics

The 155 new patients and the 672 visits on which we have based this study represent but a small amount of the work of the surgical clinics and the fracture clinic during five months. These clinics had a total of 14,555 visits, of which 1,380 were the first visits the patients had made for the current surgical complaint. To get an approximate idea of the actual work of the clinics, the observations we have classified should, roughly, be multiplied by twenty, since this study includes only 10 per cent of the new patients and only 5 per cent of all the visits to the clinics. In addition to treating this large number of patients, the physicians, during five months, took part in the instruction of 64 medical students of the College of Physicians and Surgeons, ten nurses from the Hospital School of Nursing and three interns.

Something of the difficulty of the study worker's task may be estimated from the fact that in connection with the 155 patients she held nearly 1,500 interviews with patients alone, making a record of each, and as far as possible observed and recorded almost 2,000 orders. As several of the study patients were present at the same time, and observation sometimes took place in more than one room of the clinic during the same session, it is evident that the record of difficulties experienced is an understatement, and that the facts elicited must be regarded as characteristic rather than exhaustive.

THE PATIENTS

Before following the 155 patients through the clinic, we will first consider them as human beings. We believe that the problems of management that they represent are fairly typical and must be considered by all clinics treating similar groups of patients.

Occupation—There were ninety-four wage-earners—sixty-five men and twenty-nine women, between the ages of 15 and 65. Six of the women were married and had both home and business duties. Half of the men and two thirds of the women wage-earners were not married. Of the remaining sixty-one patients studied—twenty-three were women who were homemakers, twenty-nine were school children, seven were children under school age, one was a young woman dependent because of poor health, and one was a dependent widower of 57.

Nativity—Ninety-five of the patients (61 per cent of the whole group), were native born. Sixty came to America from other lands and fourteen had difficulty with the English language.

Residence—Forty-eight per cent of the 155 patients lived within walking distance of the hospital. 42 per cent within the radius of a 5 cent fare. 8 per cent paid a double fare and two patients made no

trip by train Eleven patients made at least one visit by taxi because of the severity of their condition

Economic Status—From the data which we have on ninety-five patients, we found that 23 per cent had no financial responsibility except for themselves There is wide variation in the weekly wage received by this group, since one patient received \$12, one \$40, and six between \$15 and \$25 and all maintenance

The remaining 77 per cent of the group of ninety-five patients were members of families whose total income ranged from \$10 to \$90 a week, and again there was wide variation in the number of persons dependent on the same amount of salary The most frequent wage was between \$30 and \$35 (nineteen families), and the number living on this wage varied from two to ten persons, although the family of three occurred

TABLE 1—*Types of Diagnoses in Cases of One Hundred and Fifty-five Patients Treated in Minor Surgical Clinic*

Diagnosis	(94) Wage Earners		(23) Home Makers		(29) School Children		(9) Other Dependents	
	Num ber	Per- centage	Num ber	Per- centage	Num ber	Per- centage	Num ber	Per- centage
Infection	41	44	4	17	8	28	1	11
Injuries	34	36	4	17	19	66	6	67
New growths	3	3	4	17	1	3		
Miscellaneous medical conditions	5	5	3	13				
Varicose veins	3	3	2	9				
Unclassified	5	9	6	27	1	3	2	22
	94	100	23	100	29	100	9	100

most frequently (six of nineteen) It is evident that the consideration of wage without responsibilities gives an inadequate idea of the economic status of the family to which the patient belongs, since the ability to purchase medical care varies enormously within the same amount of income

Surgical Complaint—One hundred and nine of the 155 patients studied had never been treated at the Presbyterian Hospital prior to the occurrence of the surgical disability These patients presented greater problems of management, since they required more explanation and more direction Five were old patients who returned because of a recurrence of a condition for which they had previously been treated in the surgical clinic of the Presbyterian Hospital Forty-one were old patients of the Presbyterian Hospital previously treated in either the surgical clinic, the medical clinic or the emergency ward, who returned because of a new complaint

Thirty-five of the whole group of 155 patients had previously been treated in the emergency ward before being referred to the surgical clinic in the outpatient department, because the fixed hours of the surgical clinic did not coincide with their needs

Disability—We do not know, of course, all the difficulties the patients encountered because of the surgical conditions from which they were suffering. But we do know that 143 were in pain or discomfort when they appeared on the waiting benches, thirty-five had come in after a sleepless or disturbed night, seven had abnormal temperature, fifteen moved a wounded limb with great difficulty, and five had been obliged to seek the help of others in getting themselves dressed to make the journey.

Sixty-five patients were totally unable to carry on their usual occupation at the time of the first visit, and twenty-nine more could work only part of the time or with greatly decreased efficiency. At least seventeen suffered financial loss from being unable to work. A change in job was made in eight cases during the course of treatment; four patients lost their jobs, three learned that they should seek some different kind of work, and one had to give up her job because her absence to attend the clinic created so much unpleasantness.

Mental Attitude—Sixty of the patients were in a state of considerable anxiety over their condition or from fear of losing their jobs or part of their pay or because of children left alone at home. Twelve of the whole number had fear of the treatment itself or the strangeness of the surroundings. The trip to the clinic had caused considerable pain to four persons. Two men hoped the waiting time would not be long since they had been working all night as watchmen and were obliged to get back on the job in the afternoon. Twenty-six patients were troubled because relatives or friends were giving up time to assist with housework, care for children or to come to the clinic as escort. The twenty-nine school children regarded the clinic with varied emotions—some were missing examinations and were afraid they would not be promoted, some were afraid the teacher would think they had been playing truant, at least four planned to make the clinic an excuse for a little extra vacation from their labors. Seven working men knew that their employers and fellow-laborers were working overtime to cover their jobs.

Collateral Medical Complaint—Fifty-one of the patients had other complaints or anxieties in addition to the complaint that brought them to the surgical clinic. Some thought they might as well get 'all fixed up at once,' and were glad that they had occasion to come to the clinic anyway so that they might ask care for other troubles. Among these complaints were 'colds,' 'rheumatic pains,' 'headaches' and 'dental defects.' Others had deviations from normal health of which they were conscious in varying degrees. Several patients who had been previously cared for in the ward or other clinics came back as old friends but with an embarrassed consciousness that they had not kept the best of their-

ment Twenty-seven had never previously sought treatment for these collateral complaints and now wanted advice Seven had "lapsed" from some other clinic of the Presbyterian Hospital, and now had complaints about the original disability or some new one, seven had recently had outside care for some collateral condition, but had "lapsed" from that care and still had complaints, five were active at the present time in some clinic of the Presbyterian Hospital, and five were under other outside care Most of these complaints were revealed spontaneously to the worker in reply to her question as to the patient's general health Others were revealed after the worker had questioned the patient about some condition for which he had been treated previously at the Presbyterian Hospital and described in the medical record

Social Complaints—Observation and brief but sympathetic inquiry as to the effect of the surgical condition on the mode of life or the earnings of the patient, revealed that in nineteen of the 155 cases some social problem had arisen from the disability or complicated the care for it The question of arranging for the support of dependents, or of being supported during the period when earning power was decreased was most important in fourteen of the nineteen cases Savings exhausted by unemployment, debt for other illness, sickness of other possible wage-earners in the family, and nonsupport by husbands, complicated the situation Not all the nineteen patients directly revealed the problem that was disturbing them One infant, suffering from an infection, was dirty and undernourished, the sister who brought the child explained that the mother was sick, and that there was no responsible person to care for the baby There was obviously a problem in connection with a frightened child who had a fracture of the radius, the mother was irritable and nagging in the clinic, and clearly had no idea of how to handle the child One mother with an abscess of the finger had sick children at home, and could not care for them and herself at the same time

In addition to the patients whose surgical condition had served to cause or to emphasize some difficulty at home, twenty-nine more revealed home anxieties which had been troubling them before the surgical condition developed For example, eight were feeling stress from the unemployment of the breadwinner, five were disturbed and the home disorganized because of illness of other members of the family Three were worrying about insufficient income for their needs We have no means of knowing how many more of the 155 patients were facing social problems of some kind, since the information on the twenty-nine cases was not solicited by the study worker, and usually was given by the patient in response to friendly questioning concerning the effect of the surgical disability on daily earnings and life We can only say that 31 per cent of all the patients studied—twenty-three wage-earners, eight

home-makers, four wage-earning housewives, nine school children, three small children, and one dependent young woman, revealed that there were more or less serious disturbances in their personal lives, although no searching inquiry was made to obtain this information.

Problems of Management—It was not the purpose of this study to analyze the surgical problems in the cases studied. As our interest was in the care of the patients as persons, we have omitted all reference to problems of surgical technic, and such difficulties of organization and maintenance of the clinic as financing, selection of a staff, etc. Certain problems in addition to those confronting the patients themselves (which are, of course, also of concern to the clinic) were brought to our attention.

Management of these patients was made more difficult in fourteen cases by the fact that the patient's knowledge of English was limited. Two patients seemed of such low mentality that it was almost impossible to make them understand instructions, two made contradictory statements, at least one exaggerated and five were so terrified as to prevent them from asking questions or giving necessary information. A number of the patients were deaf, and one so much so that he had to be communicated with in writing. One was intoxicated. One was so discouraged by life in general that he felt there was no use in carrying out treatment. Six had to be urged to tell the physicians of symptoms or complaints which were worrying them. One knew more than the physician as to what form of treatment was desirable. Two sought other care simultaneously with care given at the clinic as they did not feel complete confidence in the physician. Four children came for treatment unaccompanied by responsible persons in instances in which operation or instruction was necessary. In the case of seven children there was evidence of neglect or carelessness at home—the parents of one refused permission for an operation. At least one patient had no facilities at home to carry out the treatment ordered by the clinic. In one case dire necessity forced a man with dependents to return to work against the physician's advice. One patient was sent in from another hospital without any report as to previous treatment. Four did not seek care at the clinic until considerable time had elapsed after the injury.

Treatment—In the management of the group of 155 patients there were three definable types of clinic orders. The first type was the form that implied the consent of the patient but did not involve his active participation, such as bandaging and laboratory tests. Management in these cases sometimes involved giving the patient some instruction as to how he was to hold his arm or the need for remaining quiet, but in general some member of the staff took the active part. One hundred per cent of the patients were affected by this group of 699 clinic orders.

The second type of order was concerned with the return of the patient, or with carrying out treatment in some other department of the hospital or in another institution. Management of the patient through this administrative type of order involved some instructions and explanation of the importance or desirability of carrying out the order. Nearly 100 per cent of the patients received such orders, of which there were 994 in all.

For example, forty patients had to be referred to the operating room, with explanation and reassurance, direction to the place, and often instruction as to the signing of anesthesia permit, arrangement for relatives to accompany them home or other assistance. Seven had to produce specimens of urine or go to the laboratory for blood counts. Forty-six had to be directed to the roentgen-ray department and to have supplementary payments adjusted. Forty-seven had to procure medicines or apparatus, which made it necessary to direct them to the pharmacy, social service department or commercial concerns in addition to explaining to them the use of the article prescribed.

Thirty-six patients were referred or transferred to other clinics or departments in the Presbyterian Hospital, often to more than one department, since seventy-three orders were issued among the thirty-six patients. Three were admitted to the wards. Ten were referred for care outside the Presbyterian Hospital, and had to be given credentials and instructed as to the location of the clinics and at what hour they were to go. Five hundred and eighty return appointments were given in the clinic, which presumably involved some consultation of the patient's preference as to the hour and an explanation of the appointment card. A reduction of the fee was granted in fifteen cases after discussion of the patient's ability to pay. Eight loans were made to patients who had no money with them.

The third type of order was given to the patient to carry out at home as part of his treatment. Eighty-five of the group of 155 patients were given such orders, thirty different orders being given in all. Some of these were in the form of prohibitions—as in forty-nine cases, orders not to go to work—and these involved inquiry into the kind of work, telling the patient the order and notifying him when he could modify or discontinue it. Other orders involved instruction in addition to notifying the patient when he could discontinue the treatment. Examples of such orders are hot soaks ordered in twenty-seven cases, flaxseed poultices ordered in nine, and internal medication ordered in twenty-four. Questioning of the patient on each visit as to how the instructions were being carried out was also implied in this group of orders. There were 189 such orders.

To summarize, 1,882 orders were given in connection with the 155 cases (not including discontinuance orders) and 1,183 (63 per cent),

involved instruction and the securing of the active cooperation of the patient. Six hundred and ninety-nine (37 per cent) implied the consent of the patient, but did not involve any direct instruction or any participation of the patient. The 1,882 orders did not include any clinic activity prior to the examination of the patient by the physician and to make a complete total one must add activities in connection with admission, assessment, making out of record taking of history and the clerical work made necessary by handling the record on each visit.

TABLE 2—*Clinic Orders to Patients to Be Carried Out at Home **

	Patients	Carrying Out			
		In Full	Partly	Not	Unknown
Total	189	113 (60%)	21 (11%)	18 (10%)	37 (19%)
Refrain from usual occupation	49	39	4	0	6
Rest part affected	13	8	3	0	2
Hot soaks	27	14	5	2	6
Stay in bed	4	2	0	1	1
Icebags	4	2	1	1	0
Apply heat	4	1	0	0	3
Flaxseed poultices	9	2	5	1	1
Keep dressing wet	12	8	1	3	0
Protect with dressing	1	1	0	0	0
Force fluids	1	0	0	1	0
Avoid jumping in school	1	0	0	0	1
Use cane	1	0	0	0	1
Use crutches	1	1	0	0	0
Wear suspensory	1	0	0	0	1
Wear different kind of shoe	1	0	0	0	1
Cut toe-nail straight across	1	0	0	0	1
Keep warm	2	1	0	0	1
Keep hand dry	2	0	1	0	1
Use rubber glove	1	0	1	0	0
Have head shaved	1	0	0	1	0
Stay out in air	1	0	0	0	1
Drink eight glasses water	1	0	1	0	0
Keep leg elevated	1	0	0	1	0
Do exercises	1	0	0	1	0
Bring letter from physician	1	0	0	1	0
Apply external medication	13	12	0	1	0
Use mouth wash	2	1	0	1	0
Take internal medication	21	21	0	0	0
Wear elastic stockings	7	0	1	0	6
Wear elastic bandages	2	0	0	0	2

* The thirty different kinds of advice were given to eighty-five patients.

ACCOMPLISHMENTS OF CLINIC

With what degree of success were the problems dealt with? To what extent were the orders carried out? What were the outstanding difficulties experienced along the way by both patient and clinic?

Disposition of Cases.—Ninety of the 155 patients (58 per cent) carried on their treatment for the original surgical complaint until discharged by the clinic either as improved or to seek care in one of the clinics of the Presbyterian Hospital or in some other institution. Sixty-two (40 per cent) lapsed and three (2 per cent) were still active at a year. The discharged improved patients had been in care an average of fourteen days during which they had averaged 5.8 visits.

The "lapsed" patients had been under care an average of sixteen days and had averaged 4.4 visits before lapsing. The "transferred" patients had averaged 1.9 visits in 5.3 days in the surgical clinic to which they originally applied.

We have incomplete information on the sixty-two patients who did not finish their treatment. Four of the whole group of sixty-two wrote in response to a follow-up that they were "cured" and had returned to work. Using the last note on the chart and the study worker's notes as a basis, the chief of clinic was able to estimate the condition of fifty-one of the sixty-two "lapsed" patients. He considered that forty-one were improved, six probably improved and only four not improved. No attempt was made to follow up the fifteen patients who were transferred to other care after the contact was established, so we do not know how many of these subsequently "lapsed."

Collateral Medical Complaint—Of the fifty-one patients who had collateral complaints (several of them more than one) at the time they were admitted to the surgical clinic, only ten were already under treatment; ten others were considered and treatment arranged for spontaneously by the physician in the surgical clinic. In forty-one cases little or no consideration was given to the collateral condition by the physician in the surgical clinic, and this was usually either because he did not read previous entries on the charts of old patients, or because he did not read the entire history as taken by the study worker and written on the chart. Thirteen of these cases were called to his attention either directly by the study worker or by the patient after being urged by the worker, and treatment was arranged. Eighteen patients who were not already receiving treatment left without any care for the collateral complaint. We cannot say how many of these were not considered by the physician, but it is our impression that in the majority of cases no inquiry was made of the patient, although the complaint was noted on the chart by the worker when she took the history.

On the other hand, some collateral medical conditions which had not been revealed to the study worker by complaints of the patient were discovered or suspected by the physician in the clinic, since twenty-three patients besides the twenty-three already described were transferred or referred by the physician to other departments or institutions, and some of these patients were referred or transferred for care of collateral conditions.

Collateral Social Problems—At least forty-eight of the 155 patients were worrying about some social problem which, in nineteen cases, was created by, or connected with the surgical disability. In the majority of cases it was never elicited by any one officially connected with the

clinic, since no social inquiry was made of the patient except the routine question as to his ability to pay the fee.²

Nine of the forty-eight patients reached the social service department, only four of them having been referred spontaneously by the clinic. In addition to the nine, seven who had no problems were referred to the social service department to purchase apparatus, so that the total contact of this department was with sixteen of 155 patients and only eleven of these (7 per cent of 155) had a spontaneous contact.

Carrying Out of Orders—(a) Some of the orders did not involve the active cooperation of the patient but had to be carried out by some member of the clinic staff. Of these 699 orders (of which 557 were for dressings), 98 per cent were carried out by the staff. No attempt was made to estimate the quality of the performance except in a few cases in which some difficulty was caused the patient.

Subordinates were handicapped in carrying out orders in several cases by the fact that they had not received direct instruction from the physician, since he had dictated his orders and the record was not clear. The physician was often inaccessible because he was teaching or operating.³ We found a number of instances in which subordinates acted without instruction, and in the majority of cases it was because the physician was inaccessible.

(b) In carrying out the group of orders involving some cooperation on the part of the patient two elements are included: first, a clear understanding by the person who was to give the order and second, comprehension by the patient of what he had to do and its importance. Seventy-nine per cent of the 1,183 orders involving cooperation on the part of the patient were carried out in full according to the best information at hand. For example, sixty-five of the seventy-three orders were carried out in the case of patients referred or transferred to other clinics or departments in the Presbyterian Hospital and eight of the ten orders that patients be referred or transferred to other institutions. We do not know what took place in the case of the other two. Thirty-eight of forty operations that were recommended were performed and in sixty-four out of sixty-five cases roentgenograms were made. In 4 per cent we have no information. 17 per cent were known not to have been carried out in full.

2 At the time of the study one social worker was on duty in the outpatient department and as a routine all patients who were referred for admission to the ward or for whom apparatus was ordered were sent to her desk for advice and assistance if necessary. Other patients were referred to her at the direction of the physicians in the clinic or of the superintendent.

3 In one general surgical clinic the physician personally directed the department but gave instruction to students, operated and supervised the staff for admitting new patients and was also ordered to be available for the

(c) The 189 orders given the patients to carry out at home in connection with the treatment are included in the 1,183 that we have just analyzed. The study worker was obliged to rely on the patient's statement, of course, in judging the degree of accuracy with which orders

TABLE 3—*Analysis of Clinic Orders*

	Individuals Affected	Ordered	Carried Out	Not Car- ried Out	Unknown
Orders Not Requiring Instruction of the Patient	Total	699	681 (98%)	15 (2%)	
Surgical dressings	92	557	547	10	
Pressure bandages	7	14	14		
Strapping	9	18	18		
Splint	7	13	13		
Slings	3	6	6		
Cast	2	2	2		
Soaks in clinic	1	3	2	1	
Irrigation with surgical solu- tion of chlorinated soda	2	2	2		
Massage in clinic	4	21	20	1	
Baking in clinic	3	3	3		
Antitetanus serum	6	6	5	1	
Autogenous vaccine	1	9	9		
Epinephrine	1	1	1		
Cultures	23	23	23		
Wassermann tests	11	11	10	1	
Letter or report	10	10	10		
Orders Requiring Explanation or Instruction (in clinic)	Total	994	820 (82%)	165 (17%)	9 (1%)
Operations	40	40	39	2	
General anesthetics	27	27	27		
Local anesthetics	9	9	9		
Urinalysis	7	7	7		
Blood counts	2	2	2		
Röntgen ray examination	46	65	64	1	
Securing medication and ap- paratus					
Internal medication	24	24	21	3	
External medication	13	13	12	1	
Elastic stockings	7	7	1		6
Elastic bandages	2	2		1	1
Crutches	1	1	1		
Patient referred or transferred to other care	46				
In Presbyterian Hospital	33	73	65 (89%)	8 (11%)	
Baking and massage clinic		19	18	1	
Radiotherapy clinic		4	4		
Wards		3	3		
Medical clinics		7	6	1	
Skin clinic		2	2		
Dentistry or oral surgery		10	5	5	
Other surgical clinics					
Women's		1	1		
Fracture		3	3		
Surgical diagnostic		8	8		
Social service		16	15	1	2 (20%)
Outside Presbyterian Hospital	10	10	8 (80%)		
Manhattan Eye and Ear		3	3		1
Orthopedic Hospital		3	2		
Vanderbilt Clinic		1	1		
Neurological Institute		1	1		1
Cornell Clinic		1	1		
Compensation physician		1	1		
Appointments	Total	683	534 (78%)	149	
Appointments given in clinic	138	580	483 (83%)	97	
Written appointments	64	103	51 (50%)	52	
Loans	8	8	8		
Admitted without paying	7	8	8		
Reduced fee	15	15	15		

were carried out at home, direct observation might have revolutionized some of the figures. In this group, the largest number of patients given any single direction was forty-nine, who were told not to engage in their usual occupation. Thirty-nine of these, we believe, carried out the order

in full and four in part, we have no information concerning six. Twenty-seven were ordered to apply hot soaks, fourteen did as directed, five failed to do so, information is lacking in eight cases. A summary of this whole group of orders given to the patient to carry out at home showed that 60 per cent were probably carried out as directed. 21 per cent were not carried out, and information is lacking on 19 per cent.

PROBLEMS FACED BY PATIENTS

Difficulties Encountered—Fifteen of the 155 patients went through the course of treatment without any difficulties being noted. Most of the difficulties appear to have occurred during the first visit which seems to indicate that the greatest need of attention to managing the patient is on admission and throughout the first visit.

The principal difficulty experienced by patients was due to lack of adequate instruction. Forty-eight of the eighty-five patients who were given advice to carry out at home revealed to the study worker that they did not fully understand the advice itself or were uncertain as to how long to continue it. For example, in twenty instances the correct use of soaks was not fully understood, in twenty-five instances, patients did not understand whether they could go on with their regular occupation or not, four more had received conflicting advice from physicians as to whether they should work.

Instruction of patients as to other orders was also inadequate in thirty-one instances. This failure to instruct the patients was aggravated by the fact that it was difficult for them to ask questions of the physician in clinics in which the physician passed from patient to patient dictating his notes, and then left the room to teach or to operate.⁴ The patient hesitated to interrupt, and had no subsequent opportunity to ask about his condition or treatment. Aides had the same difficulty and often had to choose between making decisions without authority and delaying patients who could not afford to spend any more time in the clinic. Ten instances were noted in which patients were seriously disturbed but were unable to speak to the physician.

The appointment system, while on the whole advantageous to the patients, raised such problems as the following: hardship caused patients by not calling them for treatment in accordance with the appointment; giving appointments at times inconvenient for patients (fourteen cases); long waits (162 instances). A follow-up of broken appointments was

4 In the general clinics the patients were called in to the treatment room in groups and the physician passed from patient to patient examining and dictating at the same time. The aide kept the records of the cases and the dictation directly on them. The nurse followed the physician and changed dressings he had prescribed. She consulted the medical record.

left largely in the hands of the aide, since the physician seldom had time to examine the charts of patients who failed to come as directed. The decision concerning follow-up was made by the physician in only nineteen of sixty-two "lapsed" cases. Five cases were lost because the appointment was not properly recorded and the record was not reviewed when the patient failed to return. The aide made the decision to drop thirty-eight of the cases.

Another group of difficulties was connected with the financial management of patients. In thirteen instances, fees were collected from patients who, in the opinion of the study worker, were not able to pay, in six of these cases she reported her observations to the superintendent's office, and revision of the rate was made, in the seven cases not reported no revision was made. It was chiefly the long duration of the treatment or disability which made revision necessary, and this was not determinable by the admitting clerk, who fixed the rate at the patient's first visit. In six cases the study worker felt that the patient was able to pay for private or pay clinic care, one of these she reported to the superintendent's office, and adjustment was made. One patient continued care in the emergency ward after the out-patient department had notified him that he was ineligible for care in the clinic and advised him to seek private care. In three instances, full fees were collected after the patient had been notified that reduced rates or free care would be granted. In two cases, no refund was made after the patient had been charged for an operation which was postponed. Two compensation cases were not discovered on admission.

Many difficulties were related to the recording of clinic orders or observations. These seldom affected the patient directly at the time, as did most of the other "difficulties" we have noted, but were rather potential sources of difficulty which might hamper his care in the future.

In 168 instances, recording of diagnosis or advice was incomplete or inaccurate.

While no attempt was made to give the patient an idea of the probable duration of his disability, the tendency on the physician's part to underestimate this might reasonably be noted here as a potential cause of difficulty. Because of the pressure on the physician's time in the clinic, little effort was made to obtain a forecast from him as to the length of time the patient must remain under treatment or the number of days that he would be unable to do his usual work, but the complete data we have on thirty-one cases seem to show that the physician's tendency was to underestimate the time necessary for treatment. The average time estimated was nine days, while the thirty-one patients were actually under treatment an average of fifteen days. The time in

eight cases was estimated correctly within a day in four it was overestimated and in nineteen underestimated

We have data on only seventeen cases about the length of time the patients were unable to work, but here we find the same tendency—the average time of actual unemployment was eleven days the average time estimated by the physician was six and one-half days. The time was correct within a day in two cases, in six it was overestimated and in nine underestimated.

The difficulties which have been discussed in this and the foregoing sections are not exhaustive. Nor have we, in this part of the discussion, stressed the degree to which these difficulties were rectified. In some cases they were discovered and adjusted by the clinic staff before the patient left, in others, the patient was encouraged by the study worker to ask the proper person to make the adjustment in a few days.

TABLE 4—Average Cost of Treatment at Clinic Rates for Various Number of Days*

Complaint	Days	Cost
30 Infections	17	\$108 each
19 Injuries (no fractures)	9	248 each
5 New growths	14	12 each
3 Miscellaneous medical conditions	15	67 each
4 Varicose veins	1	84 each
6 Unclassified	11	21 each

* This cost includes visits, roentgenograms, baking, and massage, elastic stockings, and other special items. The rates of the clinic were 50 cents a visit.

study worker herself reported the trouble to the proper person or made the necessary explanation.

The importance of the difficulties by no means centers in their number, since many more probably occurred than were brought to the attention of the study worker, but in their kind and the fact that they occur at all. The outstanding failure seems to be in the instruction of the patient as to his part in the care of his condition and in delegating to subordinates responsibilities which they are not equipped to handle.

Cost—Although the material is not complete, we have some evidence on which to base an estimate as to what the treatment has cost the patients in money and time. The figures which follow are based on 175 cases.

The average actual cost to these patients, obtained by subtracting remissions, unpaid loans, reduced rates, etc., was as follows:

Infections	\$1.08	Miscellaneous	0.67
Injuries	1.82	Unclassified	0.21
New growths	0.02		
Varicose veins	0.84		

The average cost to these sixty-seven patients at clinic rates was thus \$3 64, they actually paid an average rate of \$3 24. This was distributed over an average of 5 8 visits in fourteen days. From the data on fifty-six "lapsed" cases we found that the average cost at clinic rates, prior to the "lapsing," was \$3 04, the patients actually paid an average cost of \$2 36, which was distributed over an average of 4 4 visits in 16 2 days. The fifteen patients who were transferred were considered only until they left the clinic to which they first applied. The average cost at clinic rates was \$2 49, the average amount paid was \$2 09. To all these averages must be added an average of 43 cents for transportation.

To summarize the average cost to the 138 patients at full clinic rates would have been \$3 26, they actually paid an average of \$2 75 (84 per cent of the full rate). To this must be added 43 cents for transportation, making an average cost of \$3 18 for each person.

These averages do not include seventeen cases (11 per cent, which were not completed during the time of the study from Jan 8 to May 31, 1925), and it is undoubtedly among this 11 per cent of the cases that we find the long drawn out treatment, with corresponding elements of expense and time. The cases include such diagnoses as fractures and ulcers of the leg, and had figures been available they would have greatly affected the averages. The problems of financial management would appear much increased if studied throughout the whole course of treatment of these long-time cases.

Time—From data on 674 visits made by 132 patients, we found that the average length of time spent in the clinic on each visit, reckoned from the time the patient entered the door of the outpatient department to the time he left, including operations and visits to the roentgen-ray department but none for baking and massage, was seventy-eight minutes. To this must be added an average of forty-eight minutes for the time spent in going back and forth from home to clinic, making a total average of two hours and six minutes spent by each patient in making each visit.

By studying the figures for a number of first visits, we found that they averaged one hour and forty-eight minutes in the clinic, as compared to one hour and eighteen minutes for all groups of visits. First visits without operations or the employment of the roentgen ray averaged one hour and thirty-one minutes, first visits with operations averaged two hours and fifty-four minutes, first visits with the use of the roentgen ray averaged two hours and thirty-four minutes. It is evident that it requires careful management to avoid unnecessary delays to the patient on the first visit.

Study was made of 185 instances in which the patient was kept waiting an exceptionally long time, so that his time in the clinic reached or

exceeded two hours, and the major cause of delay was noted when it was evident. We found that in twenty-three of the 185 instances, the delay was due to operation employment of the roentgen ray waiting for massage, consultation or going to other departments and was more or less unavoidable. In forty-eight cases more the major delay was due to lateness or absence of the regular physician or to the fact that he was out of the clinic. In two cases, absence of an aide caused the delay. In eleven, the long waiting time was due to the shortage of screens or to the fact that the patient had to wait while the nurse left the clinic to get some article necessary for treatment. Teaching caused the long waiting time in forty-seven cases, and in only seven of these was the patient himself the subject of the teaching. In nineteen cases the delay was caused by failure to requisition or to send charts or by the failure of the aide to send for the roentgen-ray report or plate before the patient arrived. In two cases, the patient was forgotten and left behind the screen. In thirty-three cases, the causes of delay were too complicated to list—usually consisting of lateness in starting the clinic and general slowness throughout which affected the appointment system and was reflected in the waiting time of patients coming later in the morning.

SUMMARY

Effective Control of Most Cases—The outcome and disposition of the 155 cases show that the clinic studied exercised a relatively high degree of case control. This was proved by the fact that 58 per cent of the patients carried on their treatment until discharged by the clinic. 2 per cent were still active at the end of a year. 26 per cent were estimated by the chief of clinic to have been sufficiently improved by treatment to consider themselves cured, 4 per cent were probably improved and only 3 per cent were considered not improved. Data on which to base a decision were lacking in 7 per cent. The belief that most of the "lapsed" patients were improved was substantiated by the fact that they had made an average of 4.4 visits before 'lapsing,' while in completed cases the patients had averaged only 5.8 visits.

Another proof of the high degree of control exercised by the clinic may be deduced from the high percentage of appointments kept by the patients. Seventy-eight per cent of all appointments made (including those given patients in follow-up letters) were kept. The 'discharged improved' patients kept 94 per cent of all appointments, the 'lapsed' patients 61 per cent. Written appointments were sent to the 'lapsed' group.

Reasons for Effectiveness—The high degree of effectiveness is due to the effective organization of physicians and administrative staff, and the adequate system of records.

The use of a system of appointments made it possible to regulate attendance and to review the records of patients not reporting as directed. Clinic clerks or "aides" assisted with the management of the patients and attended to the clerical work connected with the system. Follow-up by letter or by visit from a social worker might be carried out at the physician's discretion.

The medical record was of the "unit" form so that record of previous treatment of the patient in any department of the hospital—outpatient, social service, ward or laboratory—was complete, and all the previously discovered facts concerning the patient's physical or social condition were available to the physician. The notes made in any department showed the condition of the patient at his last visit to that department, and the disposition of the case, giving the date that the patient was expected to return if the case was still open or designating it as "patient discharged," "lapsed—no follow-up necessary" or "lapsed," with the physician's instructions concerning follow-up.

Low Cost—The cost of clinic care to the patient in time and money was low. The cost at clinic rates to all patients studied (including those who lapsed and who were transferred) was \$3.26, of which, after allowing for remitted fees, an average of \$2.75 was paid. This amount with car fare made an average cost of \$3.18 a person.

The amount of time spent in the clinic by the patients compares favorably with that which they would have had to spend for private care—although the fact that the clinic was held in the morning made the loss of time more important to working people who could have sought private care at more convenient hours. An average of one hour and eighteen minutes was spent on each visit, which included actual treatment as well as waiting time. First visits when operations were not performed or the roentgen ray used averaged one hour and thirty-one minutes.

Most Patients Satisfied—When possible, the worker secured from the "discharged improved" patient an opinion as to whether he considered the treatment successful. Forty-five of the forty-nine patients interviewed believed themselves cured, three thought their condition was unchanged but had confidence that the apparatus secured would help them, only one was dissatisfied. Several expressed appreciation of the treatment, and the interviewer received the impression that the majority of the patients were pleased with the interest that had been taken in them and satisfied with the service they had received.

Explanation of Treatment Necessary—Although the conditions for which the patients were treated were generally considered "minor" it was shown that they caused considerable disturbance in the lives of these

persons, and also that treatment entailed a large number of explanations and instructions which required attention to the psychologic and social elements of management in order to render the treatment effective. The difficulties experienced by the patients indicate that not enough attention was paid to making instructions clear, since 56 per cent failed to understand directions for home treatment either as to the process itself or as to the length of time it should be continued.

Undiscovered Social Problems—The principal difficulties experienced by the patients were due in general to the fact that they were not sufficiently individualized. In particular, the general health and social aspects of each patient were not usually discovered unless the patient took the initiative, and psychologic factors in management were neglected.

The question might well be raised as to whether it is the responsibility of a minor surgical clinic to discover and handle these situations. Clinic management has not yet developed to the point at which special clinics are organized and run in such a way that the constitution and general condition of each patient can be studied. Full histories are not taken, the staff is inadequate.

Planning of Clinic Procedure Required—In connection with these collateral medical and social complaints it would appear that even a brief inquiry into the patient's health and social situation and some history of his previous medical experience, made at the time of his admission to the outpatient department and assignment to the clinic for treatment would give the necessary clues for instigating medical and social care and would remove from the special clinic the burden of inquiry.

A plan of clinic procedure that would allow a minimum of three or four minutes of the physician's time for each case and give the patient an opportunity to ask questions would go far toward removing blinited impressions and misunderstandings. The form of clinic management employed in the clinic for cases of fracture in which the physician, with the chart before him, called in one patient at a time to treat him, led to greater concentration and better individualization of the patient. The other form of clinic management employed in the general surgical clinic in which the patients were called into the treatment room in groups and the physician passed from patient to patient dictating his notes as he went made possible the direct attention for a larger number of patients but did not make it possible to give attention on one person. Had this physician been supplemented by a more responsible aide serving as a nurse, so many difficulties as it was experienced would not have been put in the hands of clerical workers who were not a necessary part of the clinic care.

CONCLUSION

From such studies as this, we are beginning to realize the meaning and the possibilities of scientific management of the patient in clinics. Further observation will reveal further needs, and only such observation will make it possible to appraise the service rendered, to analyze and to develop technics of management, and to train personnel competent to support and supplement the physician in carrying on the practice of medicine among patients in the clinic.

APPENDIX REPORT OF A TYPICAL CASE

Case XYZ, 1,000,000 has been selected as typical, and the report shows the form in which the material was collected and recorded. The summary sheet was made out on the first visit of the patient, except for the statistical summary of the time and expense involved, which was added after the case was completed. The sheet on which each visit was recorded was written up after each visit, from notes made by the worker while the clinic was in session, supplemented by study of the chart after the clinic was over. The case is copied exactly except that on the original visit sheets the time and cost of each visit appeared beside the orders and difficulties. For convenience in reproduction, they are given separately.

SITUATION PRESENTED

Patient's Name, XYZ			
Patient's Number 1,000,000		How referred, New patient	Doctor H
Age, 27	Man	Single	Occupation, hall boy
		Nativity, United States	
<hr/>			
Diagnosis	Acute lymphadenitis of superficial and upper deep cervical lymph glands		
Problem faced (including disability)	Acute lymphadenitis complicated by infected root of tooth in upper jaw and temperature of 100.3 F. Operative procedure involved and temporary bed care, with supervision and treatment in surgical and dental departments. Temporary total inability to work.		
Forecast			
	Recovery, 2-3 weeks		
	Treatment, 2-3 weeks		
	Pain, 24 hours after operation		
	Work, 5 days total inability to perform usual occupation after operation		
Proposed plan of treatment			
	Bed, soft, diet, forced fluids		
	Dentistry		
	Operative procedure when condition has broken down		
	Dressings, and supervision by surgical clinic		
Social and economic situation			
	Patient, a hall boy, alternating shifts. Earns \$5 a week and \$3.4 a day in tips.		
	Patient and mother occupy an apartment.		
	Patient's brother in good business in New Jersey.		
Summary			
Length of treatment in clinic		10 days	
Visits		10	
	Surgical clinic	6	
	Dentistry	1	
	Oral surgery	3	
Time to and from clinic		3 hours	
Time in clinic		5 hours 16 minutes	
Time lost from occupation for disability		13 days	
	Before admission	3 days	
	After admission	10 days	
Cost of treatment in clinic		\$6.75	
	Roentgen ray	\$2.75	
	Admission	4.00	
Car fare		.60	
Cost of time lost from work, unknown			
Broken appointments, 0			
Disposition, discharged improved			

SITUATION PRESENTED-Continued

Patient's Name, XYZ

Patient's Number, 1,000,000

Age, 27

Man

Single

How referred New patient

Nativity United States

Doctor H

Occupation full box

XYZ Date 1925	1 000 000 Advice and Treatment	Agent	Difficulties	Overcome	Agent
3/11	(1) Refer dental department	(Advice given by doctor)	Patient very nervous, weak and shaky, seems only faintly bright. Voice shakes during interview.	Mother is instructed to	Refer patient to dental department
Men's surgical clinic	(2) Go home to bed (3) Forced fluids (4) Flaxseed poultices (5) Soft diet (light) (6) Return to surgical clinic, 3/12		Never before ill, does not take the advice to go to bed seriously. Mother says it is hard to keep patient quiet. Patient's mother much upset and worried about patient's condition.	Worker improves on patient the importance of following instructions.	
			Mother does not understand what patient can eat.	Worker advises her to talk with doctor who explains that diet is not absolutely clear, possible to eat.	
			Mother does not understand how to treat patient at home.	Doctor explains patient is to go to bed and have flaxseed poultices which mother says she knows how to make.	
			Alde does not consult doctor as to urgency of dent appointment and gets appointment for next day.	Worker asks doctor who says patient should see dentist before going home to bed. Alde arranges appointment for next morning.	
			Doctor did not dictate return appointment to Alde.	Worker asks doctor.	
3/11 Oral surgical clinic	(7) Roentgenogram of teeth (8) Return to dental department 3/16	Dental Roentgen ray department	Patient not directed to cashier with Roentgen ray slip. Patient not directed to dental Roentgen ray department.	Worker directs.	
	2 Repeated 3 Repeated 4 Repeated 5 Repeated (9) Do not eat too much food until temperature subsides.	Worker visiting home	Observations on home visit made by worker and reported to doctor. Patient not in bed at 10:00 sitting up. Patient has drunk only 2 glasses of water. Patient had for lunch bowl of beef soup, soft boiled eggs, tea, toast, french fries and crackers. Mother has started ready to cook for 3:00 p.m.	Worker directs patient to go to bed at 10:00. Worker directs mother to stop cooking.	
			Mother has downy face, will do as patient tells her. Patient tells her she is weak, shaky, does not feel very bright.	Worker directs mother to stop cooking.	
			Mother says she is not sure if patient is better.	Worker directs mother to stop cooking.	
			Mother says she is not sure if patient is better.	Worker directs mother to stop cooking.	

Patient's Name, XYZ Patient's Number, 1,000,000 Age, 27 Man		SITUATION PRESENTED—Continued				Doctor H Occupation, hall boy	
Date	Advice and Treatment	Agent	Difficulties	Overcome?	Agent?		
3/12	2 Repeated	Surgical clinic doctor	Patient late in coming to clinic because of weakness Patient felt very sick in night Roentgen ray report not sent from dental de- partment Surgery aide did not look up	Mother kept poultice on all night Worker suggests report be shown doctor Aide gets it, and reports dental department felt tooth should be ex- tracted as soon as possible			
	3 Repeated						
	4 Repeated						
	5 Repeated						
	9 Repeated						
(10)	Return to oral sur- gical department 3/13						
(11)	Return to surgical clinic 3/13						
			Aide changes oral surgery appointment from later date, but does not record change on chart				
			Patient's mother still disturbed over condi- tion Says she was told elsewhere that he had tuberculous throat		Doctor explains that this is possible but not probable		
3/13	Removed upper left first molar, roots infected, curetted	Oral Surg	Patient late in arriving Mother states patient felt too weak to get up				
Oral Surg	(12) Return to oral sur- gical department		Patient came to surgical clinic first as he did not understand appointment		Worker directs him to oral surgery		
3/13	2 Repeated? (no record)	Surgical clinic	No return appointment recorded on chart	Aide states patient given reappointment for 3/14			
	3 Repeated? (no record)						
	4 Continue						
	5 Repeated? (no record)						
	9 No record						
(13)	Return to surgical clinic 3/14						
3/14	3 Continue? (no record)	Doctor					
Surgical clinic	4 Repeated						
(14)	Return to surgical clinic 3/16						
3/16	Remaining piece of tooth extracted	Doctor					
Oral sur- gery	(15) Return to oral sur- gery 3/20						
3/16	3 Continue	Doctor Aide					
Sur- gical	(16) Return 3/19 (changed to 3/20)						
			Patient asks to have surgical clinic appoint- ment changed to correspond with next oral surgical department appointment Aide does not consult doctor about change of appointment	Appointment changed by aide			
3/20	Roentgen ray of tooth	Dental Roentgen ray					
Oral Surg							
3/20	3 Continued (implied)	Doctor					
Sur- gical	(17) Return to dentist						
clinic	(18) Discharge						
(19)	Return to work Discharged improved						
			Patient did not pay any admission to surgical clinic Aide did not request cashier's receipt				

TABLE 5—Time and Cost Summary on Case XYZ 1,000,000

		Time of Patient			Cost to Patient			
	Date	Time to and From Clinic	Time in Clinic	Other Time Lost From Work	Cost Trans- porta- tion	Cost in Clinic	Cost in Time Lost From Work	Other Cost
Surgical clinic	3/11/25	30 min	85 min	4 days before admission	\$0 10	\$0 50	Unknown	Roentgen ray examination \$2 50
Oral surgery	3/11/25					0		
Surgical clinic	3/12/25	30	23	1 day	0 10	0 50	Unknown	
Oral surgery	3/13/25	30	90	1 day	0 10	0 50	Unknown	
Surgical clinic	3/13/25		5			0 50	Unknown	
Surgical clinic	3/14/25	30	30	1 day	0 10	0 50	Unknown	
Oral surgery	3/16/25	30	30	2 days	0 10	0 50	Unknown	
Surgical clinic	3/16/25		13			0 50	Unknown	Roentgen ray examination \$0.25
Oral surgery	3/20/25	30	30	4 days	0 10	0 50	Unknown	
Surgical clinic	3/20/25		10			0	Unknown	
		3 hrs	5 hrs 16 min	13 days	\$0 60	\$4 00	Total cost	\$2 75 7 25

ORGANIZATION AND ADMINISTRATION OF CLINICS IN THE OUTPATIENT DEPARTMENT OF THE PRESBYTERIAN HOSPITAL*

Plant—The greater part of the space in the outpatient department of the Presbyterian Hospital was apportioned during the morning hours for the care of general surgical cases—two rooms for the men's surgical clinic, two for the women's surgical clinic, one for the children's surgical clinic and three for the fracture clinic. The remaining space was allotted to the surgical diagnostic clinic and other specialties. Waiting space for patients of all these clinics was provided in the main waiting-room. A Pharmacy, operating-room (for minor surgical operations) and laboratory (for outpatient work) were in the outpatient department; the roentgen-ray department was in the main hospital.

Treatment Hours—Surgical clinics in the outpatient department were held daily except on Sunday from 9 o'clock until about 12:30. Patients applying for treatment during other hours or on Sunday were cared for in the emergency ward and given a return appointment to the surgical clinics in the outpatient department.

Staff—The chief and assistant chief of clinic were members of the attending staff of the Presbyterian Hospital under the director of surgery. Three other physicians were on duty in the four clinics studied; two were members of the teaching staff of the College of Physicians and Surgeons, and one was an intern of the Presbyterian Hospital. (Each intern spent about two months in a surgical clinic, and during the course of the study three different interns served in succession). The administration of the outpatient department was under the superintendent and the assistant superintendent of the outpatient department.

Each clinic had a pupil nurse under the direction of a supervising instructor (or her assistant) and the immediate supervision of the physician in the clinic. These nurses usually spent two weeks in each clinic.

Each clinic had an "aide" or clerk. The aide was a paid member of the clerical staff. In three of the clinics that were studied the aide was assisted by a volunteer under her direction. In one of the clinics there was no paid aide during part of the study, and the work was divided between two volunteers. Before the study was completed a paid aide was installed to replace one of the volunteers.

A member of the social service staff was on duty in the outpatient department during clinic hours. Patients were referred to her from the clinics.

* This scheme of organization and administration of the outpatient department was made from January to June 1925. No changes have since been made.

A cashier, an information-admitting clerk, a chief file clerk and two assistants, two stenographers, a statistician, a laboratory technician and three porters composed the rest of the general outpatient staff which served all clinics

Reception of New Patients—New patients were directed by a door-man to a waiting bench, where they were given blanks to fill out which contained identifying items—name, address, age, sex, etc. The information-admitting clerk assisted them in filling out the blanks, if necessary. She questioned them as to income and obligations and decided whether they were financially eligible for clinic care and whether a reduction of fee was indicated. An admitting physician (one of the surgeons serving for a designated part of the session in addition to his other duties) assigned each patient to the proper clinic. The patient then passed to the record window where his clinic card (with spaces for days and hours for appointment on the back) and history sheets were made out. His name was cleared with an alphabetical file to verify his statement that he had not been a patient in the institution before. An alphabetical card with identification data was made out for every new patient. From the record window the patient passed to the cashier's window to pay his fee, and was then directed to a waiting bench in front of the clinic to which he had been assigned.

History—History-taking procedure differed during the time of the study. In the men's, women's and children's general surgical clinics it was customary for the aide to come out to the waiting benches and ask the new patient his chief complaint, its duration, cause, previous treatment and past history if she thought it relevant. This history she wrote directly on the medical record. In the fracture clinic the history was usually taken by the physician or by a medical student under supervision.

Method of Conducting the Clinic—In the general clinics the aide called the patients for treatment in groups of ten or more, according to the size of the rooms in the clinic, and seated them in chairs in a row. The order of appointment of the old patients, or the order of arrival of the new patients was observed as far as possible by the aide in calling the patients, but shortage of screens, delay in arrival of medical records or roentgen-ray reports, necessarily affected the order in which patients were called. The aide arranged the medical records of the patients on her desk in the order in which the patients sat. When all the chairs were filled, the physician went from patient to patient asking supplementary questions on the history and examining the part affected. He dictated to the aide his notes of observation, treatment prescribed and the return date, and she wrote the notes in longhand on the record. The nurse followed the physician, doing the dressings as ordered, and consulting the chart, if necessary. The aide recorded the day and hour of

the return appointment in a book and on the patient's card made out laboratory slips or roentgen-ray requisitions and arranged for the patient's transfer or reference to other departments or institutions. When the physician had dictated the data concerning all the patients he returned to do certain dressings or to assist the nurse. By the time the patient was ready to leave, the aide had made any necessary appointments for him and gave him his appointment card and any directions needed. When two rooms in the clinic were used the first one was usually cleared and ready for a new group of patients while the last dressings were being done in the second room. The process of filling the rooms and treating the patients in groups was then repeated.

In the fracture clinic the patients were called in one or two at a time and seated at the physician's desk. He read the records, talked with each patient, and made the examination at the time or later if the patient had to go behind a screen. Practice as to dictation differed among the physicians in the fracture clinic but in general they made their own notes, leaving the aide free to make appointments, to arrange for necessary roentgen-ray work and to take care of cases in which the patients were referred to different departments or institutions.

A system of appointments was in operation in all departments.

Records—The "unit" form of medical record was in use. All treatment of patients was recorded chronologically on one record and all reports of tests, all correspondence, roentgen-ray reports, etc., appeared in the record. This applied to all departments of the hospital including the ward and social service department. On each visit the physician's notes gave condition, recommendations and disposition—including the date that the patient was expected to return.

In the fracture clinic a diagnostic and follow-up file was kept of patients under care, and it was possible to learn the status of each case by consulting the file. As patients with fracture usually remain under supervision for many months, sometimes several years, such a file was necessary. It was taken care of by the aide. In the general surgical clinics the appointment book was the only index of the patients.

All records of patients were brought to the clinic by messenger. The aide requisitioned in advance records of patients expected for appointments. Records of new patients or of old patients returning for appointment were sent to the clinic by messenger as the case required. The chart numbers of patients who had no appointments were kept in the clinic and transmitted the information to the file clerk.

Use of Social Service—Patients for whom treatment was ordered by apparatus or who were referred for dressings to the social service department were dictated to the social worker's desk by messenger. The social worker used the resources and for assistance referred the patient to the appropriate department. Apparatus was ordered by the physician and the patient was referred to the

worker Other patients were referred to the social worker for inquiry or assistance at the discretion of the physician or the superintendent

Teaching—Student nurses received practical instruction at all times from the physicians in charge of the clinics Interns were under the supervision of a regularly appointed surgeon Teaching of students from the College of Physicians and Surgeons took place on four days a week The physician in charge of the men's surgical clinic and the chief of clinic or assistant chief of clinic, one of whom was usually on duty in the fracture clinic, gave this instruction The dean of the College of Physicians and Surgeons was present one morning a week in the fracture clinic during the academic year as instructor and another morning as consultant

General—There were variations in the clinics at the time of this study The women's surgical clinic was handled by three different interns during the five months of the study The children's surgical clinic—not a large one—had no full-time physician, but was visited at intervals by physicians from other clinics The fracture clinic was in the hands of the chief of clinic, or the assistant chief of clinic and one other physician The men's surgical clinic was in various hands during the time of the study as the physician usually in charge was absent part of the time from illness In the men's surgical clinic one physician taught medical students as well as examining and treating patients, often simultaneously, using the students to take the histories and assist with the dressings He was on duty certain hours for admitting new patients, assisted in the children's surgical clinic, and was on duty in the operating room

METHOD OF SUMMARY*

CARD No 1

Name Number	A Problem	B Orders	C Difficulties to Patient	D Difficulties to Clinic
Diagnosis		Clinic 1 2 3 4 etc	I Caused by condition	Over come? Agent?
Classification	Disability?		II Caused by treatment	
How referred			III Caused by medical management	V Difficulties to medical management
Collateral medical problem Previous treatment?	Handled by clinic?	Patient 1 2 3 4 etc		
Collateral social problem Previous treatment?	Handled by clinic?		IV Caused by administrative management	VI Difficulties to adminis- trative management
Physicians Disposition Patient's opinion of progress				

* A summary of each case was made on two 5 by 8 cards arranged as illustrated All items were written in full except the difficulties, which were coded

METHOD OF SUMMARY *

CARD No 2

Name						
Number	Disposition					
Age	Number of broken appointments	Number of visits	Rate	Cost at rate	Rate to patient	Cost to hospital
Sex	Number days under treatment	Special tests				
Civil status	Apparatus					
Usual occupation	Transportation		Total cost at rate		Total cost	
Usual wage					at rate	
Usual family income	Miscellaneous					
Number persons in family	Number days totally disabled		Cost at regular rate of pay		Total cost	
Other resources	Time to and from clinic					
			Cost of time at		Total cost	
	Time in clinic		regular rate		at rate	
	Total time					

SPECIAL STUDY OF DIFFICULTIES ENCOUNTERED

The difficulties encountered in connection with the giving of treatment were grouped under two main headings—those encountered by the patient, and those encountered by the clinic.

The difficulties experienced by the patient were those caused by

- (1) The condition itself (such as pain, inability to employ, loss of occupation, etc.)
- (2) The treatment for the condition (such as absence from work, part of a mother with young children whose care must be taken, expense)
- (3) Failures in medical management (such as giving wrong instructions). With this group were included certain failures in recognition which constituted potential or not actual difficulties. An example would be failure to approve apparatus secured by the patient, the responsibility of deciding whether patients who did not keep their appointments should be followed up.
- (4) Failures in administrative management (such as failure in transferring patients from one department to another, failure in the record-keeping system, etc.)

The difficulties experienced by the clinic were of two general types:

- (1) Those which interfered with the patient's cooperation on the part of the patient.
- (2) Those which disturbed the clinic's work, such as addresses or patients' failure to appear for treatment.

TABLE 6—*Difficulties to Patient, Instances and Comments*

	Patients Affected	Comments
Caused by Condition		
Physical		
Pain or discomfort	143	
Sleeplessness	35	
Temperature	7	
Swelling	20	
Bleeding	3	
Weakness	1	
Limitation of function	15	
Interference with personal care	5	
Mental		
Anxiety about		
Condition	26	
Possible loss of job	9	
Possible loss of pay	8	
Fear of treatment	12	
Social-Economic		
Interference with usual occupation		
Inability to work at all	65	
Inability to work full time	9	
Inability to work with usual efficiency	20	
Necessity of changing occupation	3	
Loss of job	4	
Loss of pay	17	(data incomplete)
Caused by Treatment in Clinic		
Physical (pain, discomfort, etc not noted)	4	
Trip to clinic causes pain	1	
Waiting in clinic nauseates patient		
Treatment during clinic hours means loss of sleep to patient, who works at night	2	
Mental		
Anxiety about		
Children at home	3	
Possible loss of job because of absence for treatment	2	
Social-Economic		
Interference with usual occupation		
Patient gives up job because of difficulty in arranging absence for treatment	1	
Danger of loss of job	1	
Time lost for treatment reduces output	11	
Reduction of income for time spent in clinic	5	(data incomplete)
Bandage interferes with efficiency	1	
Children missing school for treatment	29	
Children miss more time from school than necessary	4	
Inconvenience caused others	4	
Employer has to do extra work	3	
Fellow workmen have to do extra work		
Relatives inconvenienced by having to care for children, assist with care of home, accompany patient etc	20	
Friends inconvenienced	6	
Caused by Medical Management*		
Study and treatment		
1 Admission to wrong clinic	1	
Skin for surgical clinic	1	
Fracture for oral surgery	1	
Surgical for diagnostic		
2 History	1	Overcome by worker
Emergency ward history inaccurate	11	2 overcome by worker
Physician does not read history recorded on chart	1	
Last note not read by new physician	4	1 overcome by clinic,
Incomplete, second injury not discovered		2 overcome by worker
3 Examination	6	3 overcome by worker
Incomplete, second injury not observed		
4 Reports	4	1 overcome by clinic,
Laboratory reports not read		2 overcome by worker
No report requested from another institution which had previously treated same condition	2	
5 Instruction		
Patient does not understand		
Home treatment	20	1 overcome by clinic,
Soaks		11 overcome by worker
Medication (internal)	8	1 overcome by clinic,
Medication (external)		5 overcome by worker
Icebags	5	3 overcome by worker
Hot applications	2	1 overcome by worker
Use of elastic stocking	3	1 overcome by worker
Use of rubber finger	1	
Shing	1	
Elevation	1	Overcome by worker
Rest	6	3 overcome by worker
Exercises	3	1 overcome by clinic,
		1 overcome by worker

TABLE 6—*Difficulties to Patient, Instances and Comments—Continued*

	Patients Affected	Comments
Dressings		
Come off at home	16	
Cause pain	6	
Patient dissatisfied		
Complains house officer is rough	1	
Verbal complaint to physician about collateral condition is ignored	2	
Feels examination inadequate	1	
Not satisfied with elastic stocking	2	
Caused by Administrative Management *		
1 Instruction of patient inadequate		
Refer to other clinic	1	Overcome by worker
Need of bringing adult	1	
Release	1	Overcome by worker
Reason for postponement of operation	2	
Cost and hours of baking and massage	6	Overcome by worker
Appointment card	9	1 overcome by clinic, 6 overcome by worker
2 Directing patients		
To clinic—Patient admitted to clinic without going to cashier	5	
From clinic		
Patient not directed to emergency ward	2	1 overcome by worker
Patient not directed to operating room	2	2 overcome by worker
Patient not directed to pharmacy	1	1 overcome by worker
Patient not directed to baking and massage	1	Overcome by worker
Patient not directed to appointment desk	2	Overcome by worker
Patient not directed to dental clinic	1	Overcome by worker
Patient not directed to fracture clinic	1	Overcome by worker
3 Financial management		
Admission		
Patient admitted who, in opinion of study worker, could pay private rates	6	1 overcome by worker
Patient treated in emergency ward after refused care in outpatient department	1	Overcome by worker
Compensation case not discovered	2	Overcome by worker
Assessment		
Fees collected from patient who, in opinion of study worker, could not afford to pay	13	6 overcome by worker
Patient charged for postponed operation	2	1 overcome by worker
Cashier collects fee, although card is marked "free"	1	Overcome by worker
Card not marked "free" after arrangement for free care	2	1 overcome by worker
4 Carrying out of appointment system		
Patient not called in order	10	
Patient not consulted, hour of appointment inconvenient	11	1 overcome by clinic, 7 overcome by worker
Patient allowed to leave without appointment	2	2 overcome by worker
Appointment given without consideration of need of roentgen ray report	1	
Long delay before patient can get appointment for medical clinic	3	1 overcome by worker
Long waiting time in clinic †	102	
Broken appointment in other departments not reported to clinic	3	1 overcome by worker
5 Identification		
Change of address not noted	3	1 overcome by clinic, 1 overcome by worker, 1 overcome by clinic
Wrong address copied on chart	1	
Age wrong on chart	1	
Patient has two charts	2	
6 Recording		
Dictated notes incorrectly transcribed	9	2 overcome by worker
Anesthesia permit not attached to chart	1	
No carbon of letter written about patient on chart	2	
Incomplete note by social worker	1	
Letter from or about patient not noted on chart	5	
Diagnosis not copied on front page	1	
Appointments		
Inaccuracies in recording	31	6 overcome by worker
Follow up appointments not cancelled when patient comes in	3	
No witness on release slip	1	
7 Miscellaneous		
School children not given excuses	2	1 overcome by worker
Postponement of operation until next day because of delay in referring	2	
Conflicting instructions	1	Overcome by worker
Consideration of patient		
Exposed patient complains of cold, no assistance	1	
No effort by midt to get information requested by patient	2	Overcome by worker

* Unless noted, not overcome

† See separate study of delay

‡ Only noted here if difficulty was caused

TABLE 7. Difficulties Encountered and Comments

Table Number	Difficulty	Frequency	Comments
1	1. Patient does not come to clinic	11	
2	2. Patient does not come to clinic	1	
3	3. Patient does not come to clinic	1	
4	4. Patient does not come to clinic	1	
5	5. Patient does not come to clinic	1	
6	6. Patient does not come to clinic	1	
7	7. Patient does not come to clinic	1	
8	8. Patient does not come to clinic	1	
9	9. Patient does not come to clinic	1	
10	10. Patient does not come to clinic	1	
11	11. Patient does not come to clinic	1	
12	12. Patient does not come to clinic	1	
13	13. Patient does not come to clinic	1	
14	14. Patient does not come to clinic	1	
15	15. Patient does not come to clinic	1	
16	16. Patient does not come to clinic	1	
17	17. Patient does not come to clinic	1	
18	18. Patient does not come to clinic	1	
19	19. Patient does not come to clinic	1	
20	20. Patient does not come to clinic	1	
21	21. Patient does not come to clinic	1	
22	22. Patient does not come to clinic	1	
23	23. Patient does not come to clinic	1	
24	24. Patient does not come to clinic	1	
25	25. Patient does not come to clinic	1	
26	26. Patient does not come to clinic	1	
27	27. Patient does not come to clinic	1	
28	28. Patient does not come to clinic	1	
29	29. Patient does not come to clinic	1	
30	30. Patient does not come to clinic	1	
31	31. Patient does not come to clinic	1	
32	32. Patient does not come to clinic	1	
33	33. Patient does not come to clinic	1	
34	34. Patient does not come to clinic	1	
35	35. Patient does not come to clinic	1	
36	36. Patient does not come to clinic	1	
37	37. Patient does not come to clinic	1	
38	38. Patient does not come to clinic	1	
39	39. Patient does not come to clinic	1	
40	40. Patient does not come to clinic	1	
41	41. Patient does not come to clinic	1	
42	42. Patient does not come to clinic	1	
43	43. Patient does not come to clinic	1	
44	44. Patient does not come to clinic	1	
45	45. Patient does not come to clinic	1	
46	46. Patient does not come to clinic	1	
47	47. Patient does not come to clinic	1	
48	48. Patient does not come to clinic	1	
49	49. Patient does not come to clinic	1	
50	50. Patient does not come to clinic	1	
51	51. Patient does not come to clinic	1	
52	52. Patient does not come to clinic	1	
53	53. Patient does not come to clinic	1	
54	54. Patient does not come to clinic	1	
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57	57. Patient does not come to clinic	1	
58	58. Patient does not come to clinic	1	
59	59. Patient does not come to clinic	1	
60	60. Patient does not come to clinic	1	
61	61. Patient does not come to clinic	1	
62	62. Patient does not come to clinic	1	
63	63. Patient does not come to clinic	1	
64	64. Patient does not come to clinic	1	
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67	67. Patient does not come to clinic	1	
68	68. Patient does not come to clinic	1	
69	69. Patient does not come to clinic	1	
70	70. Patient does not come to clinic	1	
71	71. Patient does not come to clinic	1	
72	72. Patient does not come to clinic	1	
73	73. Patient does not come to clinic	1	
74	74. Patient does not come to clinic	1	
75	75. Patient does not come to clinic	1	
76	76. Patient does not come to clinic	1	
77	77. Patient does not come to clinic	1	
78	78. Patient does not come to clinic	1	
79	79. Patient does not come to clinic	1	
80	80. Patient does not come to clinic	1	
81	81. Patient does not come to clinic	1	
82	82. Patient does not come to clinic	1	
83	83. Patient does not come to clinic	1	
84	84. Patient does not come to clinic	1	
85	85. Patient does not come to clinic	1	
86	86. Patient does not come to clinic	1	
87	87. Patient does not come to clinic	1	
88	88. Patient does not come to clinic	1	
89	89. Patient does not come to clinic	1	
90	90. Patient does not come to clinic	1	
91	91. Patient does not come to clinic	1	
92	92. Patient does not come to clinic	1	
93	93. Patient does not come to clinic	1	
94	94. Patient does not come to clinic	1	
95	95. Patient does not come to clinic	1	
96	96. Patient does not come to clinic	1	
97	97. Patient does not come to clinic	1	
98	98. Patient does not come to clinic	1	
99	99. Patient does not come to clinic	1	
100	100. Patient does not come to clinic	1	

Note: 1. Noted but not overcome
 2. Only noted here if difficulty was caused

Such difficulties as the patient actually encountered in the clinic or as could be learned by interviewing him and studying his record have been carefully recorded by the study worker. There must necessarily be a large number which occurred in the home or at work which the study worker did not learn. The difficulties caused the clinic are by no means

adequately represented, and must be simply considered as illustrative. For example, a lay worker could not determine whether delay on the patient's part in seeking treatment constituted an obstacle to the clinic. One patient came to have a bullet extracted several months after she was injured, and the surgeon explained that this delay was of advantage to the clinic in this particular case. Only a few details of instructions inadequately carried out at home could be learned by the worker in conversation with the patient. Had it been possible to visit every patient and observe the method by which he carried out the instructions received, much would have been discovered. Several visits were made by the worker, and each contributed illuminating material. The record of difficulties, therefore, is by no means exhaustive, and the apparent emphasis on difficulties encountered by the patient as the result of certain breaks in technic occurring in the clinic is due not to a critical attitude on the part of the observer, but to insufficient information as to other difficulties which could not be observed at first hand.

This rough classification is the result of an attempt to analyze material which is so elusive and complicated as almost to defy grouping. Any difficulty encountered by a patient is, in the last analysis, also a difficulty to be met by the clinic, and nearly all difficulties met by the clinic are real or potential difficulties to the patient. The artificiality of the foregoing groups is therefore obvious.

In tabulating these difficulties, attention was paid, when possible, to noting whether the difficulty was overcome, by whom it was overcome—especially whether it was righted without the assistance of the study worker. As we have said elsewhere, a certain obligation was incurred on the part of the study worker by the fact that she had taken the initial history of the case, and that the patient had learned to turn to her with some of his questions. As far as possible she endeavored to play the part of observer only, but there were instances where the righting of error or misunderstanding was necessarily stimulated by her.

The element of time involved in certain situations made it almost impossible to attempt to classify difficulties on the basis of whether they were overcome, for example, if a patient leaves the clinic three days in succession without being able to ask the physician whether he can return to work, and finally gets the information on the fourth visit, can one call that difficulty *overcome*, although the patient finally receives the necessary instructions? No attempt is therefore made to state whether difficulties are overcome or not unless the conclusions are clear cut.

The difficulties are in the main tabulated on the basis of instances, not patients. The same patient might be responsible for three out of a hundred instances of failure to cooperate in carrying out orders. On the other hand, such difficulties as failure to understand the English

Worry or anxiety over financial matters would be listed only once per patient. An attempt is made to indicate where the difficulties are listed by patients and not by instances. It is important to note also that the difficulties ascribed to inadequate instruction of patients are listed without regard to whether they concern the initial instruction or the final order to discontinue. From the point of view of the patient it is not so important to know whether he can return to work as it is to know whether he must stay home from work. It is the impression of the trade worker that of the two instructions the former is the one more often selected. Effort is made to get the patient to understand that he must work his injury but he must frequently take the initiative in finding out when he can discontinue the treatment.

THIRTY-THIRD REPORT OF PROGRESS IN ORTHOPEDIC SURGERY¹

PHILIP D WILSON, M D , LLOYD T BROWN, M D , HARRY C
LOW, M D , M N SMITH-PETERSEN, M D , MURRAY S
DANFORTH, M D , RALPH K GHORMLEY, M D

BOSTON

HERMAN C BUCHOLZ, M D

HALL, GERMANY

AND

ARTHUR VAN DESSEL

ANTWERP, BELGIUM

CONGENITAL DEFORMITIES

Congenital Dislocation of the Knee Joint—Baldwin¹ reports a case of congenital anterior dislocation of the tibia on the femur. The knee was in a position of extreme hyperextension, and no flexion was possible. The condition was recognized at birth, and the deformity corrected ten days later. Under anesthesia, the dislocation was reduced with little difficulty and the leg splinted. Fixation was discontinued at the end of six months. Now, at the end of eight and one-half years, there is normal function of the knee, and the patella is fully developed. The author notes from the literature that absence of the patella has been a frequent accompaniment of this condition. He believes that the development of a sesamoid bone depends on normal function of its tendon and that in his case the presence of the patella is a result of the early restoration of function.

TUBERCULOSIS

Heliotherapy in Pott's Disease in Children—Ghormley² reports the experience of the New England Peabody Home in the treatment of tuberculosis of the spine in children, based on the study of sixty-three patients, for the most part under 10 years of age. While the diagnosis was verified in only a few of the cases by actual demonstration of the bacillus, he believes that the margin of error in Pott's disease in children is almost nil. He considers that three factors are of special importance in following progress: (1) improvement in the spinal deformity, as

¹ This Report of Progress is based on a review of 145 articles selected from 470 titles dealing with orthopedic surgery appearing in medical literature between Nov 7, 1926, and March 12, 1927. Only those papers which seem to represent progress have been selected for note and comment.

1 Baldwin, C H J Bone & Joint Surg 8 822 (Oct) 1926

2 Ghormley, R K Heliotherapy in Relation to Treatment of Tuberculosis of the Spine in Children, J A M A 88 289 (Jan 28) 1927

embolic process and that the character of the lesion of the bone is determined by the point of lodgment in the nutrient arterial system. He has reviewed a number of cases at a late period in their course and has classified the lesions on an anatomic basis as follows: 1 Subperiosteal abscess 2 Main stem of nutrient artery 3 Primary division of nutrient artery 4 Secondary division of nutrient artery 5 Terminal vessel in bone 6 Multiple processes 7 Periosteal and osteal multiple lesions

He points out that the disease may spread by secondary infections or as a result of unwise surgical procedures. The former he believes due to progressive and regressive thromboses.

Purulent Arthritis in Children—Macchi,⁵ writing on acute suppurative arthritis in infants, states that the organism most frequently present is the pneumococcus. It is almost always a secondary infection, and the primary focus in 91 per cent of the cases is an infection of the middle ear. The most frequent localization of arthritis due to pneumococcus is in the hip joint, with the knee and shoulder next. Why the hip joint is most frequently involved cannot be explained. The author suggests that it is due to the lack of resistance of the long bones, especially those of the femur, which are in the process of rapid development. Pneumococcic arthritis is almost always monarticular. The date of appearance of the lesion of the joint in relation to the original focus is variable. In the adult, it is likely to occur during the acute attack, but in children it may appear as late as ten or twelve weeks after subsidence of the attack. Gonococcic arthritis in infants is usually secondary to vulvovaginitis or an ophthalmia of the new-born. It is usually multiple, in contradistinction to its monarticular occurrence in adults. Infections of the throat, stomatitis, solution of continuity of the skin, and infections of the umbilicus are the usual points of origin for streptococcic arthritis. While in adults arthritis often occurs without lesions of the bone, it is rare in children, except in gonococcic arthritis, which ordinarily does not cause alterations in the bone. The author considers vaccine therapy valuable, but says that the vaccines should be autogenous, prepared by the method of Wright from pus removed from the joint.

SYPHILIS

Synovial Fluid of Patients with Arthritis and Syphilis—Chesney, Kemp, and Baetjer⁶ have made a study of ten cases showing clinical or serologic evidence of syphilis in which an active arthritis was present. The investigation included study of the synovial fluid with reference to

⁵ Macchi, A. *Pediatrics* **34** 1243 (Nov 15) 1926

⁶ Chesney, A. M., Kemp, J. E., and Baetjer, F. H. *J. Clin. Investigation* **3** 131 (Oct) 1926

Influence of Focal Infection on the Pathology of Arthritis—Pemberton, Cajori and Cloutei⁸ report experiments tending to show that the lowered sugar tolerance which they have so frequently observed in chronic arthritis can sometimes be corrected and a normal condition established by the use of vasodilator drugs. They consider this additional evidence that at least part of the pathologic change in chronic arthritis is due to interference with the blood supply in the smaller vessels. They point out that the observations on the blood sugar are not to be interpreted only in terms of specific carbohydrate metabolism. Glucose has been selected for study merely as the most available and easily estimated of all of the components of the blood, and is simply an expression of an alteration possibly affecting many other substances. In the light of the authors' investigations, the failure to remove glucose from the blood is probably to be referred to a failure of the blood to reach certain tissues, especially the muscles, in sufficient quantity, where under normal conditions glucose is rapidly taken up. It would therefore appear that at least occasionally the muscles of arthritic patients receive less blood as a whole than they normally should, and that therefore their physiologic function must be modified and at times much deranged. This, therefore, affords some explanation of the frequency of muscular disability in the rheumatoid syndrome and the value of exercise and massage in stimulating the flow of blood. These several observations, according to the authors, can be explained only on the assumption that arthritis is accompanied by a disturbance of peripheral blood flow, probably in the nature of vasoconstriction. This phenomenon is apparently an important result of focal infection and constitutes at least part of the pathologic process of arthritis.

Protein Arthritis—Magnuson⁹ calls attention to a type of chronic arthritis which is characterized by a stiffness in the joints which comes on after short or long periods of rest and which is relieved by exercise. The cases are not confined to any one type of individual. From the study of a group of 100 such cases, the author is persuaded that the pain and irritation are due to faulty protein metabolism. The blood uric acid was increased in 56 per cent, the blood urea in 34 per cent, and the nonprotein nitrogen in 57.5 per cent. The large majority of such patients showed improvement on a low protein diet and on increasing the elimination.

[ED. NOTE.—We believe that there is a considerable gap between the conclusions that the author draws and the observations on which they

⁸ Pemberton, Ralph, Cajori, F. A., and Crouter, C. Y. *Influence of Focal Infection and Pathology of Arthritis*, J. A. M. A. **87** 2148 (Dec. 25) 1926.

⁹ Magnuson, P. B. *J. Bone & Joint Surg.* **8** 839 (Oct.) 1926.

are based. He not only reduced the protein intake, but increased the elimination. Many clinicians hold strongly to the view that faulty intestinal elimination plays a considerable part in the causation of chronic arthritis. May not the improvement which was noted be ascribed as much to the correction of this factor as to the altered dietary regimen? The subject of dietetics in arthritis has been a controversial one for years and one must maintain a critical attitude if the mistakes of the past are to be avoided.]

The Orthopedic Principles in the Treatment of Chronic Arthritis—Swaim¹⁰ discusses proliferative and degenerative arthritis, the former having two distinct types, the infectious and atrophic. The treatment in these cases should be the restoration, first, of normal function and resistance, and second, of movement of the joints. Chronic fatigue is one of the chief factors of all arthritis, and Swaim believes that it is due to disturbances of normal function of the thorax and abdomen. The disappearance of this symptom depends on the restoration of correct body mechanics. This is accomplished by special exercises in bed to increase the capacity of the chest and to relieve abdominal congestion; resistance, and, second, of movement of the joints. Chronic fatigue is. Exercises are given together with abdominal massage. Thyroid extract is often used with benefit when the metabolism is low. In atrophic arthritis, the vapor bath of Wilde is given, with improvement in the metabolism. The author points out that a low carbohydrate diet is important if the sugar tolerance is low, that atrophic patients need an abundance of mineral salts, and usually cod liver oil. Experiments with the quartz lamp have been tried. During the acute stage, protection and rest of the joints are essential, and deformity must be prevented. After the acute stage, restoration of motion of the joints by active exercises and occupational therapy must be carried out. In the hypertrophic cases, relief of strain and protection against future strain constitute the orthopedic problem.

NUTRITIONAL DISEASES OF BONE

Intramuscular Injection of Cod Liver Oil in Rickets—By the use of intramuscular injections of an ether solution of a concentrate of cod liver oil, Wilkins and Kramer¹¹ were able to demonstrate the same changes in the concentration of calcium and inorganic phosphorus in the blood serum in cases of infantile rickets as have been found after the oral administration of cod liver oil. From this, they conclude that "whereas cod liver oil increases the absorption of phosphorus and calcium from

10 Swaim, L. T. *J. Bone & Joint Surg.* 8:845 (Oct.) 1926.

11 Wilkins, L., and Kramer, B. *Bull. Johns Hopkins Hosp.* 40:52 (Jan.) 1927.

the intestine, the fact that it is effective when administered intramuscularly indicates that this is not a purely local action upon the intestinal mucosa, but is a general one and exerted through the circulation."

Effect on Human Milk of Irradiation of the Mother—Hess, Weinstock and Sherman¹² have made a study of the effect of irradiation of the mother on the development of antirachitic properties in her milk. When the milk was given to rachitic rats, a striking difference was evident in the results obtained from milk that had been obtained previous to or subsequent to irradiation. Whereas no healing followed the first, after the latter, marked calcification of the epiphyses occurred in every instance. They conclude that ultraviolet irradiation of nursing women brings about a marked increase in the antirachitic potency of their milk. This effect is due to an augmentation in the antirachitic (nonsaponifiable) factor. The authors suggest that such irradiation be employed in order to protect infants from rickets and nursing women from excessive drain of calcium and phosphorus.

DEVELOPMENTAL DISTURBANCES OF BONE

Development of the Patella—Shands¹³ has studied the development of the patella in 100 children between the ages of 2½ and 6 years. The earliest time of appearance of the patella was 2½ years. In thirty-two cases of the group, no ossification center was present when first observed. The following abnormalities of development were noted: pointed superior borders, five cases, pointed inferior borders, three cases, double centers of ossification, two cases, roughened or depressed surfaces, six cases. Delayed ossification of the patella was present in four patients more than 4½ years of age. This was due to the following: congenital syphilis, two cases, rickets and pulmonary tuberculosis, one case, and malnutrition, one case.

Overtgrowth of Long Bones of Legs—Harbin¹⁴ reports three cases of overgrowth of the tibia and fibula. The ages of the patients varied between 12 and 14 years. The overgrowth apparently resulted from entirely different etiologic factors. In the first case, it was due to stimulation of the cartilage cells of the epiphyseal plate from adjacent osteomyelitis without invasion of the epiphysis. The second patient had a history suggesting congenital syphilis without manifestations other

12 Hess, A. G., Weinstock, Mildred, and Sherman, Elizabeth. Antirachitic Properties Developed in Human Milk by Irradiating Mother, *J. A. M. A.* 88:24 (Jan. 1) 1927.

13 Shands, A. R., Jr. *J. Bone & Joint Surg.* 8:824 (Oct.) 1926.

14 Harbin, M. Overgrowth of Long Bones of Lower Extremity, *Arch. Surg.* 14:142 (Jan.) 1927.

than a positive blood Wassermann reaction. The third case showed a generalized enlargement of the lower part of the left leg, with nerves and enlarged veins, apparently of congenital origin.

Vertebral Epiphysitis—Buchman¹⁵ reports two cases previously diagnosed as vertebral epiphysitis in which spinal deformity later developed. He regards these symptoms as proof that so-called vertebral epiphysitis is the cause and not the result of spinal deformity.

Femoral Osteochondritis and Epiphyseal Separation—Balensweig¹⁶ reports eighteen cases of femoral osteochondritis. All showed varying degrees of epiphyseal separation. Ten patients were treated by the manipulative method of Whitman, followed by plaster fixation, three, by the application of short plaster spicas with weight-bearing and two, by open operation, three were untreated. Of the manipulated cases, an excellent result was obtained in one, satisfactory in one, fair results in five, and nonunion in one. Of the two patients treated by open operation, one result was poor and the other satisfactory. The author inclines to the theory that the chief etiologic factor is a low grade infection and that traumatism and endocrine dysfunction are contributory causes. These etiologic factors bring about coxa plana in the first decade, femoral osteochondritis complicated by varying degrees of slipping of the capital epiphysis in the second decade, and osteo-arthritis in the third decade and later.

[ED NOTE—There appears to be little clinical or experimental support for the use of the term osteochondritis in designating the condition known as coxa vara of adolescence. We believe that the term epiphysolysis more accurately describes the process than any other.]

Bone Sarcoma—Summing up the present knowledge, Bloodgood¹⁷ states that in periosteal and diffuse lesions below the upper third of the femur, amputation offers more than radiation. In the aim resection offers more than radiation. If the lesion is in the upper third of the femur or is of such an extent as to rule out resection, radiation should be the therapeutic method of choice. The author advises exploration of the tumor for diagnostic purposes with immediate microscopic examination of frozen sections and a report. If this is impossible tissue should be removed with the cautery and sent to the pathologist. The author considers as the weakest point in providing proper treatment the inability to make a correct diagnosis from frozen sections so that further operation if indicated may be done at once.

15 Buchman, Joseph. Relationship Between Vertebral Epiphysitis and Spinal Deformity. Arch Surg 13 568 (Oct) 1926

16 Balensweig, I. Surg Gynec Obst 43 604 (Nov) 1926

17 Bloodgood, J. C. J Bone & Joint Surg 8 727 (Oct) 1926

Giant Cell Tumor —Goforth¹⁸ reports six cases of giant cell tumor of the bone. From a study of these cases, he concludes that the giant cell tumor is a true neoplasm, essentially benign. Under the stimulus of inadequate or improper treatment, it may recur locally. Such recurrences, as a rule, are more virulent than the primary growth, both clinically and on microscopic examination. On rare occasions, the tumor may undergo malignant transformation and may form metastases.

BACK STRAIN

Spondylolisthesis —Writing of spondylolisthesis, Asbury¹⁹ says that it is not a common condition, but that it occurs often enough to be of practical importance in the differential diagnosis of backache. The structure, embryologic formation, and function of the lumbosacral joint are factors in the causation of the subluxation. The onset of symptoms may be gradual or sudden. If sudden, the cauda equina is more apt to be injured because a sudden onset is usually associated with severe trauma. A constant feature in the history is the relief obtained from rest. On abstaining from exertion for a few days, the dull, boring back pain and radiating sciatic pain cease, only to reappear immediately on resuming work. The telescoped shortened trunk with the extreme lordosis of the lumbar spine, the concavity above the sacrum, and the prominent upper border of the sacrum or pseudokyphosis, are the outstanding features to be seen on examination of the patient. The inclination of the pelvis is lost, and the birth canal at both inlet and outlet is narrowed. Frequently, there are signs of a partial caudal lesion, but a complete lesion is rare because only the body of the vertebra is dislocated in most cases. Operative stabilization of the spine seems to be the only logical method of treatment in cases showing severe disability. This prevents further progress of the subluxation and causes the superincumbent weight to rest in a more normal line on the sacrum. This is particularly necessary in cases showing involvement of the cauda equina. In milder cases, external support seems sufficient to relieve symptoms.

MISCELLANEOUS

Painful Heel —Roederer²⁰ reviews the various theories of the pathogenesis of talalgia. Despres thought that it was due to a contusion of the cellulo-adipose tissue of the heel, resulting from prolonged standing. Duplay considered it an inflammation of the bursa under the heel, which has been described by Lenoir. Reclus, from a roentgenologic

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- 18 Goforth, J. L. Giant Cell Tumor of Bone, *Arch Surg* **13** 846 (Dec.) 1926
 19 Asbury, Eshe. Spondylolisthesis, *J. A. M. A.* **88** 555 (Feb. 19) 1927
 20 Roederer, C. *Paris med* **2** 70 (July 17) 1926

study, concluded that it was caused by bony exostosis. Roederer reports some personal cases and points out that the generally accepted view at present is that the exostosis is produced by periosteal inflammation and that it is the periosteitis which accounts for the talalgia.

Talipes Cavus from Anomalies of Dura Mater—Brechot²¹ believes that so-called idiopathic talipes cavus is primarily the result of muscular hypertonicity, with secondary contraction of the aponeurosis, tendons and ligaments. The cause is an irritation of the nerves of the cauda equina. He has explored the cauda equina in two such cases and reports finding what appeared to be a congenital thickening of the dura mater. He considers this anomaly sufficient to incite hyperirritability in the nerves. It may occur with or without associated malformations of the vertebral laminae.

Ossifying Hematoma—Stone²² has made a study of six cases of posttraumatic ossification in the soft parts and concludes that the condition is an ossifying subperiosteal hematoma instead of a myositis. In each of the cases, there was a history of a hard blow followed by a swelling, which later decreased in size. Gradually, ossification developed. Operation was performed in four out of the six cases. Each tumor was found to be bone entirely covered with periosteum. Muscle was attached to the outside, but not once was it found inside the mass. This would make it appear that following the injury there was bleeding next to the bone. The periosteum was pushed up and stretched into various shapes in which position ossification took place. Ossification was complete within two months after injury and with one exception, operation was not performed until after this stage had been reached. Good function returned promptly and has been permanent. In two instances operation was not necessary, the condition being improved by heat and massage.

[ED. NOTE—There has been a good deal of confusion in the differentiation of ossifying hematoma and myositis ossificans, and Stone's observations indicate that the former is the condition usually encountered. Operation is indicated only when disability still exists after the ossifying process has reached an end stage.]

Cervical Ramisection—Leriche and Fontaine²³ report that only slight and transient disturbance followed the severing of the last cervical and the first dorsal rami communicantes in fourteen cases. Postoperative pains were noted in 14 per cent. In one case there was pain in the temporomaxillary joint and lower teeth and in another in the acromion. Pain in the frontal and occipital regions occurred in three instances.

21 Brechot, A. *Paris med.* 2: 57 (July 17) 1926.

22 Stone, C. A. *Ossifying Hematoma*, *J. A. M. A.* 87: 1885 (Dec. 4) 1921.

23 Leriche, R. and Fontaine, P. *J. de Chir.* February 1926, p. 143.

Other sensory disturbances were rare. Muscular atrophy developed in the shoulder and hand in one case after ramisection for angina pectoris associated with tactile hyperesthesia. A slight and transient hyperemia of the nasal, laryngeal and pharyngeal mucosa, entailing brief rhinitis, hoarseness, and slight dysphagia was present in all cases. The authors conclude that the pains and muscular atrophy are the direct consequences of severing the nerves, while the headaches and sensory disturbances are the indirect result from circulatory changes after the operation.

In a second communication, Leriche²⁴ reports his observations on the effect of section of the rami communicantes in eighteen cases. He concludes that the operation does not modify the sensations of cold, heat and pain, but that it alters the mysterious internal sense of the reality of the existence of the body. He describes one case in which a man with an extremely painful amputation stump and hallucinations of painful contracture in the fingers of the missing hand was freed of all these disturbing sensations by ramisection from the second cervical to the first dorsal. The rami communicantes appear to be the vehicles for the transmission of cenesthesia, i. e., the sense of consciousness of the functioning of the organs of the body. Cases like this one suggest a new field for treatment of painful and perverted cenesthesia.

Rowntree and Adson²⁵ report a case of rheumatoid polyarthritis of six years' duration which had been resistant to all treatment. Finally, bilateral lumbar sympathetic ganglionectomy and ramisection were performed. Prior to operation the feet were cold, mildly cyanotic and sweating. After operation the pain disappeared and the feet were pink, warm, dry and comfortable. The relief persisted until the patient was last seen, two months after operation. The patient desired to have a similar operation performed on the arm.

[ED. NOTE.—The foregoing case is not interesting as an example of the way arthritis should be treated, but as an illustration of the effect, perhaps temporary, of ramisection.]

Orthopedic Problems in Leprosy—The field that leprosy affords for orthopedic treatment has been comparatively neglected. McIlhenny²⁶ has established a department of physiotherapy in the National Leprosarium at Carville, Louisiana, where there are about 250 cases, and feels that the value of treatment in preventing and correcting the deformities resulting from this disease has been demonstrated. Atrophy of the

²⁴ Leriche, R. *Lyon chir.*, December, 1926, p. 60.

²⁵ Rowntree, L. G., and Adson, A. W. *Bilateral Lumbar Sympathetic Ganglionectomy and Ramisection*, *J. A. M. A.* 88:694 (March 5) 1927.

²⁶ McIlhenny, P., *Orthopedic Problems in Leprosy*, *J. A. M. A.* 87:1888 (Dec. 4) 1926.

interossei muscles, claw foot and contractures of various types were benefited by massage, contrast baths and exercises. Ultraviolet and deep light therapy gave excellent results in nerve pain, indurated areas, old ulcers and bone necrosis. Diathermy proved of value but was dangerous when anesthesia existed in the part.

Heredity of Dupuytren's Contraction—Sprogis²⁷ has traced Dupuytren's contraction in seventeen of fifty-three persons representing five generations of one family. Among them were only two women. From his investigation he concludes that there is a marked hereditary tendency for the condition, that men are much more subject to it than women and that both parents may transmit it to their descendants. He also notes that the process involves, besides the palmar fascia, also the digital nerves, the connective tissue and the skin.

BONE, JOINT AND TENDON SURGERY

Thenar Paralysis—Lyle²⁸ reviews the various operations employed for paralysis of the thumb and concludes that a procedure combining the operations of Steindler and Ney is best. By the former operation, the tendon of the flexor longus pollicis is split and a portion turned down and attached to the base of the proximal phalanx. In the latter operation, the palmaris longus muscle when present or in its absence the flexor carpi radialis muscle, is transplanted into the tendon of the extensor pollicis brevis. When no active tendons are available an arthrodesis of the basal joint of the thumb is useful in restoring the opposing action of the thumb.

[ED. NOTE—We believe that tendon transplantation is of value when the thumb is paralyzed, and endorse the recommendations of the author.]

Operative Treatment of Scoliosis—Dickson²⁹ favors operative fusion of the spine in severe cases of scoliosis and reports the results that he has obtained by this method in twenty-eight cases. The greatest number of vertebrae fused in any one case was fifteen, the least number fused was eight. The results have been nearly uniformly successful; in only one case has the operation been a failure. Of the twenty-seven patients in whom the operation was successful none is wearing support except those recently operated on and all show definite improvement in deformity, which has been maintained without relapse. All are leading normal lives and are either at work or at school and none complains of the back.

27 Sprogis, G. *Compt rend Soc de biol* **94** 631 (March 12) 1926.

28 Lyle, H. H. M. *Ann Surg* **84** 288 (Aug.) 1926.

29 Dickson, F. D. *J. Missouri M. A.* January 1926, p. 1.

[ED NOTE—We believe that the fusion operation has a place in the treatment of scoliosis, especially in paralytic scoliosis. It should be performed only after the maximum correction has been obtained by non-operative treatment. In paralytic cases, because of the usually poor condition of the patient and the extent of the fusion, the operation is severe. We believe that the only way to avoid disaster in such cases is by thorough preoperative preparation, keeping the patient recumbent and filling him up with fluids and carbohydrates. In addition the patient's blood should be typed for transfusion, and a donor should be instantly available.]

Fascial Reinforcement of Relaxed Joints—Discussing relaxation of the knee joint, Bennett³⁰ says that there is a type of relaxation that allows normal function for the ordinary pursuits of civil life, but which does not permit the owner to participate in active athletics and sports. A stretched or attenuated anterior crucial permits outward rotation of the tibia and an increase in abduction of the tibia when the leg is in a semiflexed position. This explains the "semilocking" or "slipping out" which the patient complains of on turning with the leg semiflexed and the thigh adducted. The author has operated on eight such patients and reports the end results in six. Successful results were obtained in five, and one operation was a failure. The operation consisted of an incision parallel to the patella and patella tendon and opening into the joint. Plication of the capsule was done with fascial suture and this was reinforced by the insertion of fascial strips along the medial border. The after treatment consisted of fixation in plaster for from four to six weeks, followed by exercises to restore mobility of the joint. The only case in which a satisfactory result was not obtained was also the only case in which the internal semilunar cartilage was removed. The author reports four patients having recurrent dislocation of the shoulder treated by sutures of fascia. The operation consists of plicating the anterior capsule of the shoulder with a fascial suture, and fixing it to the acromion by passing the suture through the acromion. A Velpeau bandage was applied for four weeks, followed by gradual use. The cases reported all showed satisfactory results.

Arthroplasty of the Hip—Baer³¹ has analyzed the end results of 100 cases of arthroplasty of the hip, in which his specially prepared animal membrane has been used as an interposing substance. He describes anew the technic of his operation, and states as his reasons for using the membrane that it is easily procured, is hole-proof, leaves no muscle hernias, shortens the time of operation, and, with the membrane

30 Bennett, G. E. Fascia for Reinforcement of Relaxed Joints. Arch Surg 13 655 (Nov) 1926

31 Baer, W. S. J. Bone & Joint Surg 8 769 (Oct) 1926

now used, is not irritant. He points out that the limitation of motion after arthroplasty is usually due to shortening of the periarticular tissues. His statistics are as follows:

	Good results
19 cases of gonorrheal arthritis	95 per cent
27 cases of tuberculous arthritis	74 per cent
43 cases of septic infection	82 per cent
2 cases of fracture	100 per cent
9 cases of arthritis deformans	55 per cent

The figures for the entire group are 82 per cent good results. His criteria of a good result are: at least 25 per cent voluntary flexion, painless joint and stability in weight-bearing. In cases of gonorrheal arthritis, he advises waiting at least a year after the acute symptoms have subsided before doing an arthroplasty. In septic hips two or three years should elapse. He believes that arthroplasty should not be done in children until full growth has been attained. He feels that the most successful results from arthroplasty are obtained in the jaw and that next to this the hip yields the best results. The paper is accompanied by a complete bibliography.

[**ED. NOTE**—We consider the report by Baer of the end-results of arthroplasty of the hip in a large group of cases one of the most complete and reliable that has been made. The paper was read at the meeting of the American Orthopaedic Association and was accompanied by a cinematic presentation of the cases before and after operation and of the roentgenograms which showed good and bad results impartially. Those of the editors who heard and saw the presentation believe that Baer proved that arthroplasty of the hip is a valuable procedure in properly selected cases. His criterion of a good result is not a high one but the results as a whole regardless of what standard is used are unusually good.]

SYMPOSIUM ON ARTICULAR FRACTURES OF THE ITALIAN ORTHOPEDIC CONGRESS

At the recent Italian Congress of Orthopedic Surgeons a conference was held on the subject of articular fractures. The conclusions which were arrived at by the congress are reported by Delitala and Marcom. As these conclusions represent the most enlightened opinion of Italian surgeons on this difficult subject and are of importance not only in themselves but also in comparison with the surgical thought of other countries the editors are reporting them at more length than is usual in the *Progress of Orthopedic Surgery*.

1 The Upper Extremity of the Humerus Bloodless methods of reduction should always be used originally. Satisfactory results can usually be obtained. In incomplete fractures and in impacted fractures without displacement either of the anatomic or surgical neck, immobilization in abduction from ten to twenty days, followed by massage and movement, is the method of treatment. In fractures of either the anatomic or the surgical neck with displacement, immobilization in abduction with or without continuous traction is employed. In severe displacements, bloodless reduction under ether sometimes allows replacement of markedly displaced fragments. In Delitala's clinic, a plaster of Paris apparatus is always used, whether or not traction is employed. Immobilization does not usually exceed thirty days. Open reduction with or without osteosynthesis is reserved solely for cases of severe displacement which are irreducible or which are complicated by vascular or nerve disturbances. In recent fracture-dislocations, bloodless treatment is always attempted first. If this fails, open reduction is performed without removal of the head. Removal of the head is justified only if the fragment is very small or much comminuted. Removal of the dislocated head is, on the other hand, indicated in old fracture-dislocations. In obstetrical fractures it is well to use the hyperabduction method advocated by Whitman.

2 Fractures of the Elbow In fractures of the elbow, excellent results are to be obtained by bloodless methods. After reduction of the fracture, which is obtained (except in supracondylar fractures due to flexion) almost always by a combination of traction and flexion of the forearm associated with direct manipulation of the fracture, the elbow should be immobilized in flexion at a right angle or in acute flexion with the forearm supinated. Immobilization may be obtained by posterior plaster splints or with circular apparatus, not too tight. Lateral deviations toward varus or valgus may be better corrected with plaster of Paris apparatus. Open reduction should be reserved for supracondylar fractures with marked displacement which cannot be reduced bloodlessly. Open treatment is the method of choice in comminuted fractures with marked displacement. In fractures of the condyles and epicondyles it is not desirable to do an open operation, as it has been demonstrated that satisfactory results are not obtained, even though the anatomic reposition is perfect.

3 Fractures of the Wrist Bloodless treatment almost invariably gives satisfactory results. Reduction is done under an anesthetic. Immobilization is usually in a position of palmar and ulnar flexion. The duration of immobilization should be from fifteen to twenty days.

4 Fractures of the Upper Extremity of the Femur The fractures are usually through the neck or intertrochanteric region. Fractures of

the head, epiphyseal displacements, and subtrochanteric fractures represent only a small part. Fractures of the neck especially are characterized by their slow consolidation. According to the studies in Delitala's clinic consolidation occurs in proportion as the fracture line approaches the base of the trochanters. Of various methods of treatment, three are in greatest use: the original method of Whitman; the method adopted by Rossi (reduction, immobilization and continuous traction) and a method modified from that of Whitman. The last method is the one used in Delitala's clinic. It consists of reduction usually under a general anesthetic, and of manipulation in flexion, internal rotation, and mechanical traction, followed by fixation in a plaster of Paris spica which reaches below to the toes. The limb is held in moderate abduction (so that walking may be possible) and in internal rotation. If impaction is present, breaking up of the impaction is done only if there is evidence of good osteogenetic powers on the part of the patient. In fractures of the middle of the neck and of the neck close to the head open treatment is used at once, unless there is some contraindication in the general condition. The exposure is made through an anterior incision. The osteosynthesis is obtained by a long Lambotte screw or an autogenous bone transplant from the tibia or from the fibula.

5 Fractures of the Lower Extremity of the Femur. Only a small percentage of all fractures is represented in those of the lower extremity of the femur. In adults with recent supracondylar or intracondylar fractures with moderate displacement, continuous traction is applied for about fifteen days with the knee flexed. This usually improves the position of the fragments. The position of flexion is of great importance in this fracture. Flexion is maintained with plaster of Paris splints forming a double inclined plane, with pillows placed beneath the popliteal space, or with apparatus of the type of Zuppinger. Traction is made in the line of the axis of the thigh. Subsequently a plaster of Paris apparatus is applied with the knee in flexion. In supracondylar fractures with marked displacement direct skeletal traction is used. In intracondylar fractures with marked displacement osteosynthesis of the fracture with exact anatomic reconstruction must be used whenever bloodless methods do not give the desired reduction.

6 Fractures of the Upper Extremity of the Tibia. Practically the same methods are used in fractures of the upper extremity of the tibia as in fractures of the lower extremity of the femur—that is, continuous extension in flexion and usually immobilization. Frequently a hemarthrosis which should be aspirated is present. When the displacement of the fragments cannot be reduced bloodlessly open operation is indicated.

7 Fractures of the Patella. Open reduction is the treatment of choice.

8 Fractures of the Ankle The most frequent displacements that must be overcome in the treatment of a fracture of the ankle are the valgus position of the foot, the posterior subluxation of the foot, a certain amount of equinus deformity, and separation of the tibia and fibula Bloodless methods are those chiefly used It should be remembered that an exact anatomic reduction is necessary for a good functional result In fractures involving only the internal and external malleolus, a posterior plaster of Paris shell is usually sufficient except in cases in which there is a rupture of the tibiofibular ligaments, when a small amount of varus position is required The position of varus of the foot is the one of choice for immobilization of bimalleolar fractures and the fracture of Dupuytren If posterior displacement of the foot combined with a fracture of the posterior margin of the tibia is present, the displacement is overcome by a movement of propulsion forward of the foot The equinus position of the foot due to the contracture of the muscles of the calf is easily overcome when the reduction of the fracture is performed early When delayed even one or two days, the movement of dorsiflexion frequently causes a redisplacement of the fragments Therefore, it is opportune to overcome the equinus deformity in successive stages Open reduction of fractures of the ankle should be limited to irreducible fractures or fractures that cannot be held in position

[ED NOTE —The editors find themselves in essential agreement with these conclusions]

Motor Backfire Fractures of the Wrist —Pointing out the wide diversity of opinion in respect to the exact nature of backfire fracture, Edwards³³ reported his own conclusions based on a study of forty-two patients treated at the King's College Hospital He divides the cases according to the mechanism of the injury as follows

1 Direct Violence When the handle of the starting crank of the motor is wrenched from the hand and strikes the forearm Here the fracture may occur at any point below the middle of the forearm The most common site is about 1 inch above the articular margin The displacement is usually slight

2 Indirect Violence When the handle kicks back, with the hand on it Here there may be two different mechanisms (a) With the thumb in front and the wrist in abduction This usually results in a fracture of the styloid (b) When the thumb is placed behind the handle, in line with the fingers Here the mechanism is one of pure hyperextension, and the radius fractures at its weakest point, which is between $2\frac{1}{2}$ and 3 inches above the joint Edwards describes the treat-

33 Edwards, H C J Bone & Joint Surg 8 701 (Oct) 1926

ment he employs which conforms to the usual methods of closed reduction and splinting. Operation is advocated only in cases of long standing, when a wedged or curved osteotomy is advised. In fracture through the epiphysis, he recommends fixation for at least three weeks after reduction before massage and motion are begun.

Fractures of the Os Calcis—Harding³⁴ describes the treatment he employs in "smash" fractures of the os calcis with broadening. With the knee flexed over the end of a table reduction is accomplished by the following means. A claw retractor is embedded in the skin at the back of the heel and a stool with a triangular wedge of wood on it is placed under the foot and is screwed up so that the arch of the foot is forced upward, the forefoot being held down with the hand and downward traction exerted on the heel by means of the retractor. A cabinet maker's D clamp is then applied to the sides of the heel to correct the broadening. A plaster cast from toes to mid thigh is then applied with the knee semiflexed and the foot in equinus. This is worn three weeks. Full weight-bearing is permitted at the end of three months. The author reports that of fifteen patients treated in this manner (two of the cases were bilateral) all are at work the average duration of disability being five months.

[ED. NOTE—This method of reduction appears dangerous on account of the trauma it inflicts on an already extensively traumatized area. The results however are described as good. The fact that all the patients are reported as back at work at the end of five months makes us wonder whether it is meant by this that they are back at their old jobs and earning the same wage as previously.]

Ankylosis in One Thousand One Hundred and Fourteen Cases of Fracture—It has been claimed by those who oppose open intervention in the treatment of fractures that nonunion follows this method of treatment more frequently than it does closed methods. Those who hold this view may find support for their contention in the statistics of Newell³⁵ who has analyzed 1,114 cases of fracture epiphyseal separation and dislocation. Only 5 per cent or fifty-five patients were treated by open operation, only twenty-three of these being for injuries not compound. The author states that not a single case of nonunion resulted in the entire group. Reduction was accomplished with the aid of the fluoroscope in almost all the cases. The largest group of fractures was of the phalanges numbering 224 cases and the next largest was of the radius, numbering 103 cases.

Fracture Experience in the Norton Company—The newly opened fields of study in industrial medicine have put stress on the commercial

34 Harding, M. C. *I Bone & Joint Surg.* 8:720 (Oct.) 1921.

35 Newell, E. T. *South M. J.* 19:688 (Sept.) 1921.

value of the workman's time In the case of fractures, data must be accumulated from which estimates may be made of what represents the normal period of disability of different types of injury Clark's study³⁶ of 127 fractures in a manufacturing plant of 2,600 employees is of value principally in comparison with other tabulations that are made In a factory in which it was possible to take back the employees at the earliest possible moment by providing work of a type especially adapted to their injuries, the average time lost was thirty-eight days This showing appears satisfactory, but the article carries the suggestion that it ought to be possible to shorten the period further

The Operative Treatment of Fractures—Soudder³⁷ feels that closed methods in the treatment of fractures have been perfected to the point that further development along this line cannot be expected If further improvement in treatment is to occur, it will result only from refinement and development of the operative method of treatment Technical improvements in the future will lessen the risk of operation just as they have already in the past Even now the ever widening expansion of operative treatment is being witnessed Soudder feels that already it is possible to say, in respect to certain fractures, that operative treatment is the method of choice He proceeds to summarize the advantages of operative treatment in general and to indicate in as much detail as possible the conditions in which he considers operative treatment necessary It is not possible to summarize these, and they should be read in the original article

RESEARCH

Comparative Studies of Synovial Fluid and Plasma—From a comparative study of the synovial fluid and the blood plasma in twenty-three cases of articular lesions of known pathologic changes, Allison, Fremont-Smith, and Kennard³⁸ have determined the relation between the protein, chloride, sugar and nonprotein nitrogen content of the two fluids The protein contents of the fluids is less than that of the plasma, and the chloride content is greater in the fluid This is the same relationship that holds in pleural fluid, peritoneal fluid and in cerebrospinal fluid The sugar content in noninfected fluids from fasting patients is slightly lowered, while in bacterially infected fluids the sugar is markedly lowered In two cases of tuberculous disease of the joints, the sugar content was moderately lowered The authors suggest that the determination of the sugar content may be of considerable diagnostic value

36 Clark, W I Boston M & S J 195 1064 (Dec 2) 1926

37 Soudder, C L Boston M & S J 195 1187 (Dec 28) 1926

38 Allison, Nathaniel, Fremont-Smith, Frank, Dailey, Mary Elizabeth, and Kennard, Margaret J Bone & Joint Surg 8 758 (Oct) 1926

Ischemic Contracture—Jepson³⁹ has made a comprehensive review of the literature on "ischemic" paralysis and reports the results of animal experiments to reproduce this lesion. By ligation of the femoral vein combined with incision across the middle third of the thigh and the use of a constricting bandage, he was able to produce the condition in dogs. However, when the incision was drained the lesion did not develop. He discusses the pathologic changes observed in man and points out that the condition may develop with or without the use of bandages, splints, etc. That the tension due to extravasated blood and serum is an important factor seems clear, and he suggests that early drainage may be of value.

[ED. NOTE—Jepson's observations confirm the conclusions of Brooks that venous obstruction is the important causative factor. The latter produced the lesion in the isolated muscles of dogs, while the former has produced it in the entire limb.]

Growth of Long Bones in Childhood—Harris⁴⁰ has made a study of the growth of the long bones. He has observed the rate of growth in a child of 106 weeks, in whom the growth began at the age of 32 months. He states that his observations confirm the experiments of Hunter and Duchamel and clearly show that there is no intercalated growth—that is, growth from the center, in the diaphysis of the long bones. Transverse striations are shown to be manifestations of cessation of growth. These occur normally in adolescence. They may occur with seasonal variations in the rate of growth or in cases in which there is marked arrest in the rate of growth due to acute illness or starvation. They occur in rickets as part of the healing process. There are three processes normally concerned in the formation of new bone—cartilage proliferation, cartilage calcification and degeneration, and ossification proper. These three processes are related to (1) a water soluble growth-promoting vitamin or vitamins, (2) the enzyme of Robinson or vitamin X, and (3) the fat soluble vitamin or vitamin A. The author states that the term "growth-promoting," which is commonly used in connection with vitamin A, is a misnomer since the true growth-promoting vitamins are water soluble. He also believes that any conclusions concerning methods of curing rickets which are based on the lime test are fallacious, as cessation of growth is the factor that determines this.

Brittle Bones and Blue Sclera—Key⁴¹ has observed a case of brittle bones and blue sclera and has made a study of the bone material obtained by operation. From this he concludes that the underlying process is in

39 Jepson, P. N. *Ann. Surg.* **84**: 785 (Dec.) 1926.

40 Harris, H. A. *Growth of Long Bones in Childhood*. *Arch. Int. Med.* **35**: 785 (Dec.) 1926.

41 Key, J. A. *Brittle Bones and Blue Sclera*. *Arch. Surg.* **13**: 523 (Oct.) 1924.

"hereditary hypoplasia of the mesenchyme," which name he applied to the whole syndrome. He emphasizes the fact that the condition is hereditary and gives in detail a review of the literature on this question. In contrast to osteogenesis imperfecta, the fractures in this condition are not numerous and do not appear at birth. Deformities are common due to malunion of the fractures, and there is an unusual laxity of the joint structures. The bones show marked brittleness. The laminae are irregular in arrangement, and the amount of compact bone is decreased by the presence of numerous large canals. This probably accounts for the frequency of fractures. The author feels that the condition described does not resemble osteogenesis imperfecta, the latter not being hereditary. From idiopathic osteopsathyrosis, the differentiation is not so clear. Here heredity again distinguishes the condition. He offers the following classification of idiopathic bone fragility:

- 1 Hereditary form—hereditary hypoplasia of the mesenchyme
- 2 Nonhereditary forms
 - a* Osteogenesis imperfecta
 - b* Osteopsathyrosis with white sclerae
 - c* Osteopsathyrosis with blue sclerae
- 3 Probably not hereditary—osteosclerosis fragilis generalisata or marble bones

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ISOLATED GIANT CELL XANTHOMATIC TUMORS OF THE FINGERS AND HAND

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The isolated giant cell xanthomatic tumors arising from the tendon sheaths and other soft tissue of the extremities have been of clinical and pathologic interest for many years. Despite considerable study their true pathologic classification is still in doubt and unfortunately they are too often diagnosed giant cell sarcoma. The clinical picture of the tumors is well established, however, and should have some bearing on the consideration of the pathology. They are characterized microscopically by the presence of two striking elements: the foreign body giant cell and the foamy cell; once seen, this combination is never forgotten. When one considers that for many years both these cells have been shown to be nonspecific and to occur in the most diverse types of lesions and that their presence denotes the fact that foreign material is present, one must look for other factors to determine the malignancy or benignancy of the tumor.

Xanthomatic tissue appears in many forms, not only as single isolated growths but also associated with various medical conditions and as a disease of the skin, xanthoma multiplex. In many instances the latter conditions have been shown to be associated with hypercholesterolemia and this possibility must not be ignored in considering these growths. Pinkus and Pick in 1908 and later in 1910 showed that there was increased cholesterol in the blood in xanthoma multiplex and in other types of xanthoma but they thought that the isolated tumors were true neoplasms and were not associated with such an increase. Several extensive discussions of the whole subject of xanthoma have appeared recently and to these the reader is referred (Clegg 1925, Weber 1925, Winstmann 1925, Stewart 1925). In his textbook Kohnstamm discusses xanthoma under three subheads: xanthoma, xanthoma multiplex and xanthoma or tumors. Peckham

presence of an increased blood cholesterol in xanthoma multiplex although he remarks that not all cases show such an increase. He does not suggest that such an increase is present in the xanthoma en tumeurs but he does not classify this condition with tumors of the tendon sheath, though he does remark that they are greatly similar in pathology. Stewart gives a brief but excellent summary of the growths containing foamy cells, and divides them into two large groups, those with an increased blood cholesterol and those without such an increase. To the first group he adds the various dermatologic manifestations of xanthoma (xanthoma palpebrarum, xanthoma multiplex, xanthoma planum, xanthoma tuberosum and other forms), xanthomas occurring in diabetes, renal and hepatic disease, the strawberry gallbladder, the cholesteatomas of the choioid plexus and arterial atheroma. To the second group he assigns the myeloid kidney, myeloid tumors of the tendon sheaths (which he thinks are endotheliomas), retention cysts of the breast, cerebral softening, dermoid cysts, mycosis fungoides, certain thyroid lesions and such foamy cell deposits as occur in subacute and inflammatory conditions. Levy (1925) also separated the tumors of the tendon sheath from the xanthelasmas accompanied by hypercholesterinemia. Weber (1924) thought, however, that they are all associated with an increased blood cholesterol. Cases of xanthoma multiplex have been reported in which no such high cholesterol values have been found (Rosenthal and Braumisch, 1921). The evidence for hypercholesterinemia in the isolated tumors is inferential. We have not found any published results of such an increase in any of these tumors.

The first reference in the literature to the yellow tumors is by the French dermatologist, Rayer (1835), who pictured in his textbook the yellow plaques of the eyelids (xanthoma palpebrarum). Lebert (1845) noted the yellow color of these soft tissue tumors and gave the name "xanthos" to the coloring substance, which was thought at the time to be a peculiar fat. Addison and Gull (1851) described five cases of multiple xanthoma associated with liver (jaundice) and pancreatic (diabetes) disturbances. Paget, in his "Lectures on Surgical Pathology" (1853), described the pathologic picture of the yellow tumors which he notes as coming from various tissues, the breast, cerebral membranes, subcutaneous tissues and the uterus. The earliest references to the yellow giant cell tumors of the tendon sheaths are from Broca (1860) and Czerny (1869). The majority of the early references are in the French literature, in which are found two good reviews of these isolated tumors, the earlier one by Heurtau (1891), who considered only the giant cell tumors of the tendon sheath, the other by Tournay (1913), who collected reports of all cases of tumors of the tendon sheath, among them fifty-four reports of the giant cell type. It is probable that many

of the cases collected by Tournoux were of the xanthoma type though they were not so recognized at the time (Garrett 1924)

At the suggestion of Dr A B Kanavel, we took up the study of these tumors and have eight cases to report four of them from the service of Dr Kanavel at Wesley Memorial Hospital Chicago one from Dr H M Richter, one from Dr J R Buchbinder one from the late Dr William Schroeder and one from Dr W H Woolston who began the study of these tumors on the service of Dr Kanavel and who collaborated in the study

REPORT OF CASES

CASE 1—Mrs D, aged 54, a housewife, was operated on in March 1919 for a small tumor of the size and shape of a bean on the distal phalanx of the left little finger. The tumor was smooth, firm and freely movable under the skin. It had appeared four years previously and was caused she thought by irritation



Fig 1—The tumor in case 3 (Mr R). It lay on the ulnar side of the right index finger, was smooth, lobulated and had the consistency of a fibroma. It was not connected with the tendon sheath.

from a ring on the finger next to it. Three years before the operation she had caught the tumor between two boxes and this trauma had stimulated its growth. During the year before operation it had grown more rapidly. At operation a yellowish encapsulated tumor was found. It lay in the subcutaneous tissue and did not show any connection with tendon sheath, joint or bone. Microscopically it was a characteristic xanthoma (figs 9 B and 14 C). There were large areas of xanthoma cells (fig 9 B, I C) and numerous giant cells of the foamy body type. Many small blood vessels were seen, such as one might expect to see in chronic inflammatory tissue (fig 14 C). Blood sinuses were present but not abundant and hemosiderin was seen in moderate amount. Scattered isolated groups of xanthoma cells were noted. There was no evidence of alveolar formation in the tumor. The tumor has not recurred after complete local removal.

CASE 2—Mrs W, aged 53, a housewife, was operated on in September 1920, eighteen months after the second pregnancy. She had a tumor on the ulnar side of the right index finger which had developed at this place while previously she had used a ring on the

except the thought that it might be malignant. At the time of operation an encapsulated tumor was found attached to the tissues over the first and second phalanges, but apparently not to the tendon sheaths. A frozen section was made at the time of operation, and the diagnosis returned was giant cell sarcoma. After this the finger was amputated along with the head of the third metacarpal bone. The microscopic section (figs 5 C and 11 A) revealed a tumor a great deal like that in case 1, polymorphic in its cells and in its make-up. Some areas were trabeculated (fig 5 C), and many endothelial cells and fibroblasts were seen, often filled with pigment. Recent hemorrhages suggested the origin of the pigment, which gave a Berlin Blue reaction for iron. Giant cells were numerous, but the xanthoma cells were not so frequent as in case 1. Blood vessels were not plentiful and tended toward the adult type. There has been no recurrence to date.

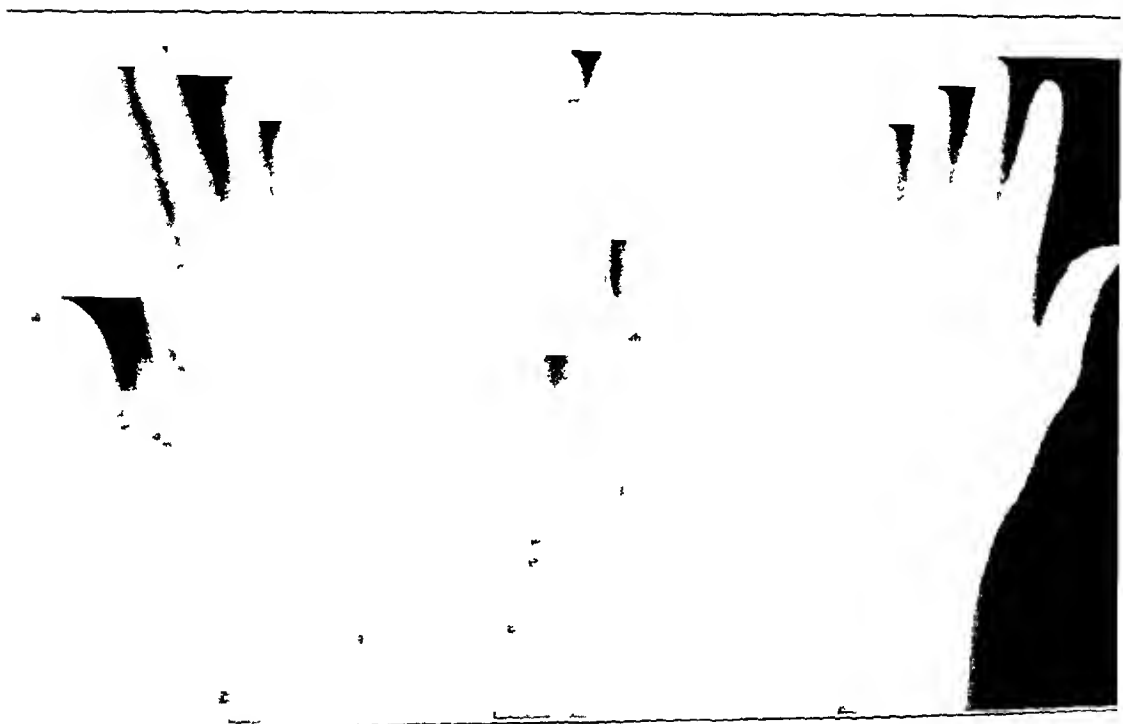


Fig 2—The tumor in case 6 (Mother A). It lay on both volar and dorsal surfaces of the right wrist and had involved tendon sheaths, joint capsule and bone. It was removed in two stages. Previous to the first operation it was thought to be tuberculous.

CASE 3—R, between 50 and 60 years of age, a tradesman, was operated on in February, 1921, ten months after a smooth lobulated tumor (fig 1) had appeared on the right index finger, following injury with a bowling ball. In the interval before operation the tumor had grown to the size of a walnut. It caused no pain or functional disturbance. The tumor was freely movable under the skin and did not move with the tendons. At operation it was found to be well encapsulated and to be attached to the fibrous tissue on the ulnar side of the finger, and it did not involve the tendons or tendon sheaths. It was smooth and lobulated, and on cut section had the peculiar yellow areas so characteristic

of the xanthomas. There was no infiltration of the bone. On microscopic examination (figs 6 *A*, 10 *B* and *C* and 11 *B* and *C*) the picture was polymorphic: a connective tissue capsule sent down into the tumor numerous trabeculae (fig 6 *A*), which divided it into alveoli containing various sorts of cells. If trabeculae were not present throughout the tumor but in the deeper parts were replaced by an amorphous material which contained fewer cells. The giant cells (figs 6 *A* and 11 *B* and *C*) were of all types, sizes and shapes and contained as many as a hundred or more nuclei; some foamy giant cells such as Spiess described, were seen (fig 11 *C*). Foamy cells were liberally scattered throughout the tumor, both as small isolated groups and as large areas. Cholesterol crystals (fig 10 *C C C*) were seen in the central parts of the tumor. We were not able to get an unfixed section of the tumor to see whether it contained crystals of

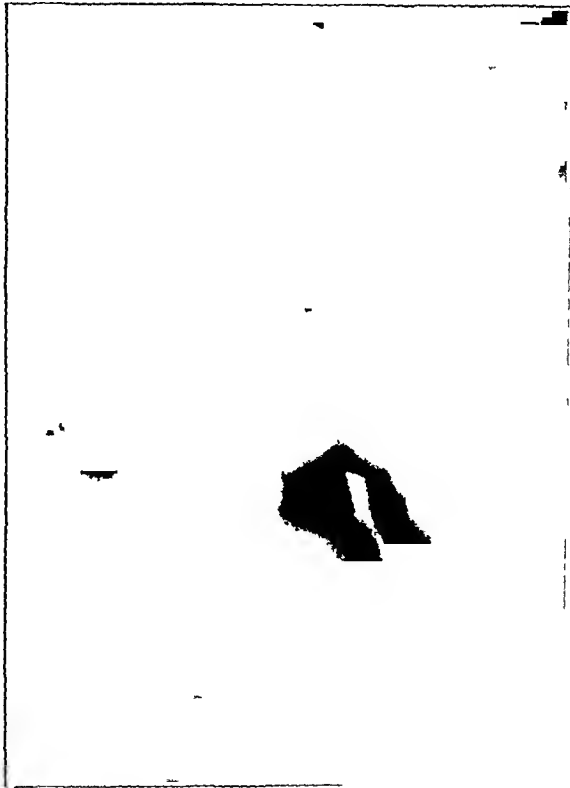


Fig. 3.—The hand in case 7 (Mrs. G.). The tumor lay on the outer side of the right middle finger. The skin was not involved, and no care was taken. Tendon sheath was made out. Microscopically it was a typical xanthoma.

cholesterol, although this observation has been contradicted, since the vessels were numerous and of the adult type. Erythrocytes were not infrequently frequent. Some pigment was present but no red cells were seen. No round cell or polymorphic infiltration was seen. It was removed since its removal six years ago.

CASE 4.—Mrs. W., 40 years old, 20 years old. The tumor was a small tumor which had been slowly growing for many years but had not caused pain. It was removed by excision.



Fig 4—Photomicrographs of sections through the tumors *A* (case 4) A distinctly encapsulated tumor which contained no xanthoma cells, but a great number of giant cells The capsule, *C*, is shown surrounding the tumor and sending into it strands of connective tissue which tend to lobulate it, *C'* Bands of connective tissue and fibroblasts ran throughout the tumor, *C''* Many giant cells, *GC* and *GCT*, were seen, giving the appearance of a giant cell tumor of the bone *B* (case 8) Two giant cells, *GC*, lying in a connective tissue and fibroblastic group of cells The alveolar formation was noted here *C* (case 4) The group of giant cells *GC*, under high magnification showing three large giant cells, *GC*, and numerous other small ones lying in an alveolus, with other types of cells, probably endothelial, *EC*, and *FB*, fibroblasts

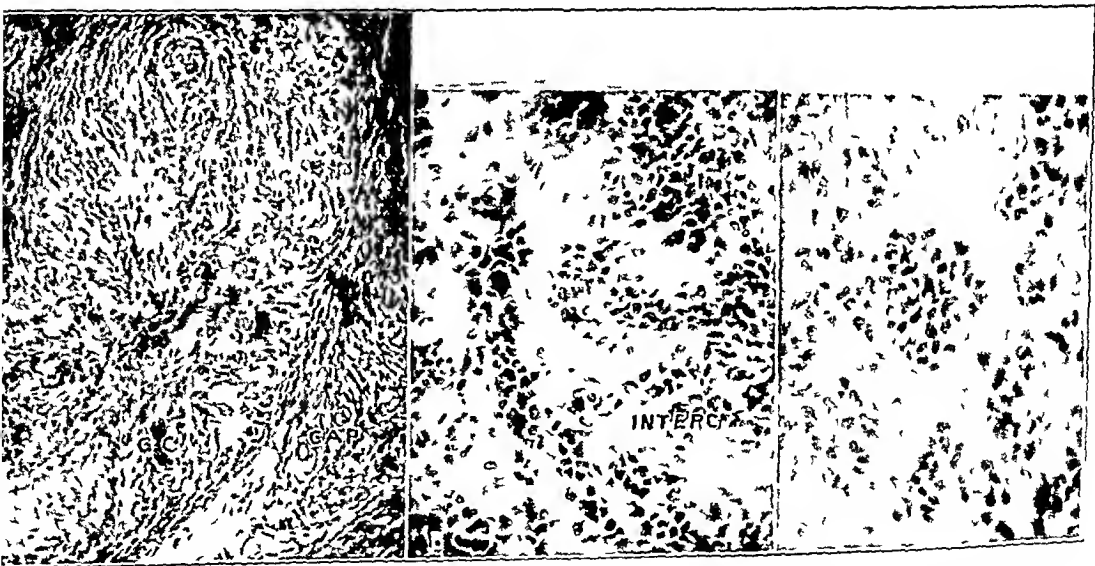


Fig 5—*A* (case 7) An area from the tumor made up of confusing whorls of spindle cells and connective tissue, that might easily be taken for a fibroma A few giant cells, *GC* and some small capillaries, *CAP* were seen *B* (case 4) This shows the amorphous intercellular substance, eosinophilic, *INTERC*, which contained a few nuclei The other cells were fibroblastic and endothelial *C* (case 2) A somewhat similar area in another tumor An alveolus, *AL* was noted, containing what appeared to be endothelial cells

a nephew, a physician, she had it removed in October 1921. It seemed to be attached to the synovial membrane of an interphalangeal joint. Microscopic section (figs 4 *A* and *C* and 5 *B*) showed that a thick connective tissue capsule (fig 4 *A*) sent trabeculae down into the tumor, dividing it into many smaller lobules. In many instances these trabeculae were fibroblastic (fig 5 *B*). Endothelial cells (fig 5 *B*) and giant cells (fig 4 *C*) were frequent. Areas of pigmentation were seen at the periphery of the tumor, but no area of hemorrhage were noted. Xanthoma cells were not seen, since but one section of the tumor was available for our examination, we cannot say that foamy cells were absent, as we have noted that they are often absent from parts of a tumor while they are numerous in other parts. The tumor has not recurred to date.

CASE 5—S., a dentist, aged 31, was operated on in July 1924, about a year after a small tumor had appeared on the palm of the right hand at the place where his extraction forceps rested. It was firm, lobulated and not fluctuant, and was apparently attached to the palmar fascia. It was somewhat tender. For a while it had grown slowly and without pain, but recently it had taken on more

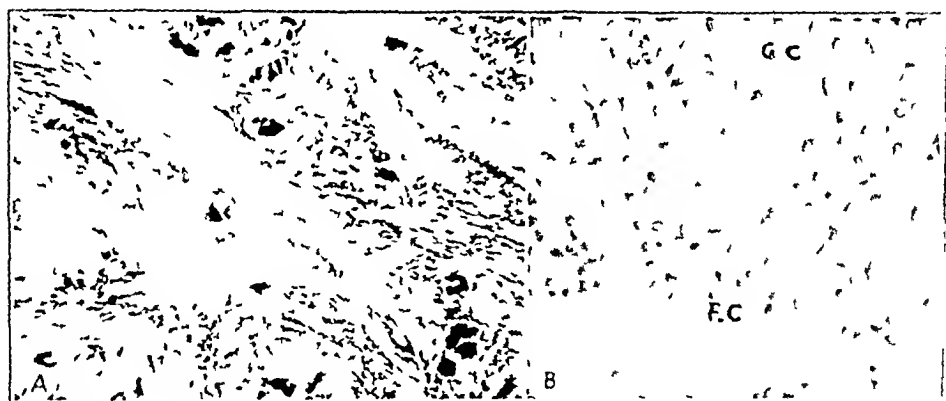


Fig. 6—1 (case 3). In this section the strands dividing the tumor into lobules were more adult in type. Numerous giant cells were seen in the field. *B* (case 6). An endothelial cell group from the tumor. The flat endothelium and the vesicular body are well shown. A foamy cell *GC* and a group of cells *EC* are also shown.

rapid growth and had attained the size of a hazelnut. At operation the tumor growth was seen to be attached to the palmar fascia, the tendons being normal. Microscopically it was a typical xanthoma with xanthoma cells, fibroblasts, endothelial cells, and some deposition of cholesterol. It has not recurred to date. The results of three cholesterol determinations on the blood of this patient are shown in table 1. No crystals of cholesterol were found (the cholesterol determinations were made after the tumor was removed in 1924).

CASE 6—Mother A., a nurse, aged 55, had developed a tumor on both the volar and the dorsal surfaces of the fingers of the right hand previous to admission. It had been present for several years. Operation was first performed in February 1922. The tumor had grown more rapidly, the fingers were stiff, and the skin of the fingers was present in places where it should not have been.

tenosynovitis was striking, and the growth was diagnosed as such before operation. It was large, nodular and soft, was over both the volar and dorsal surfaces of the wrist and, from external examination, seemed to involve the tendon sheaths. The skin was freely movable over it. The volar mass was the first to be removed in February, 1926 (fig 2). The volar mass was composed of yellowish granulation-like tissue involving the tendon sheaths but not the tendons. It lay under the volar carpal ligament and on the pronator quadratus and had involved the metacarpocarpal joint of the thumb. The radius was also somewhat involved. Microscopically (figs 6 *B*, 7 *A* and *B*, 8 *A*, 9 *A*, 10 *A*, 12 *A*, *B* and *C*, 15 *A* and *B* and 16 *A* and *B*) the mass was cellular, there was no demonstrable capsule and numerous endothelial cells and fibroblasts were seen. The blood vessels were of the adult type in many instances, but in places were seen those changes described by Bellamy that led him to think that the vascular endothelium was proliferating to produce the tumor. These changes are shown in figure 12 *A*, *B* and *C*. Sinuses

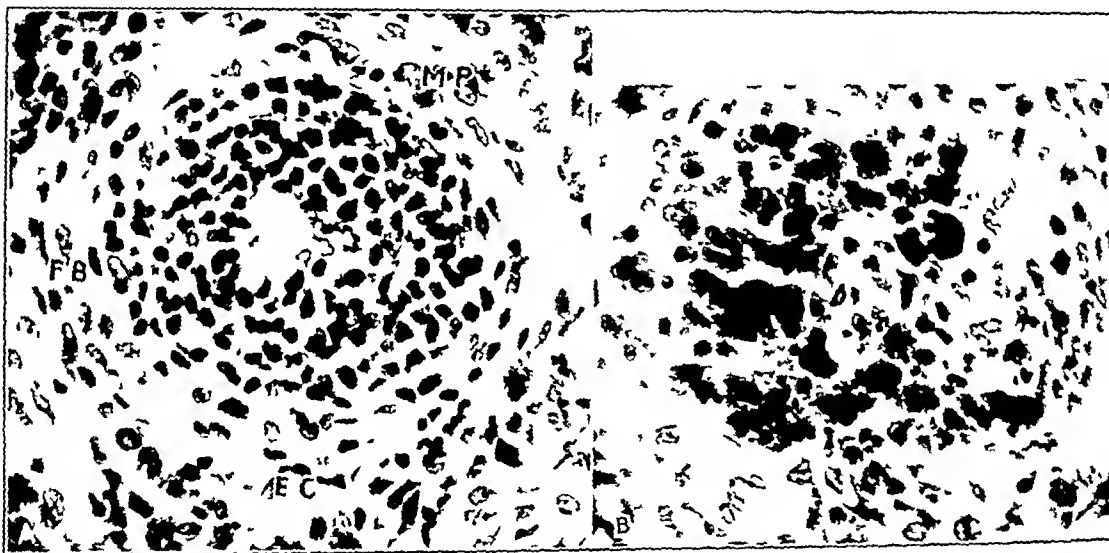


Fig 7—*A* (case 6) A small vessel with marked perivascular round cell infiltration. Farther out were fibroblasts, *FB*, endothelial cells, *EC*, and large mononuclear phagocytes, *MP*. *B* (case 6) An area of deposition of pigment granules, which gave a positive Berlin blue reaction, were both intracellular and extracellular.

were present in this part of the tumor, but were not so prominent as they were in the second part removed. Vacuolated endothelial cells were noted throughout the tumor (fig 6 *B*). Large phagocytic cells, at times full of pigment, were noted in all parts of the tumor. The pigmented areas seemed to be somewhat circumscribed and appeared to have resulted from small areas of hemorrhage into the tissue (fig 7 *B*). Fresh areas of hemorrhage were noted. Foamy cells (figs 8 *A*, 9 *A* and 10 *A*) were frequent, both as large groups and as small isolated accumulations. They appeared to develop from endothelial cells by a process of gradual vacuolization. Giant cells were scarce (figs 6 *B*) and small having but few nuclei; some of the cells contained pigment. A striking characteristic of this tumor, not noted in the second part removed seven months later, was the great number of eosinophils throughout the mass. They seemed to have infiltrated

the whole tumor and did not lie in masses or groups or with any particular arrangement. They were not noted in any other tumors seen by us.

The dorsal parts of the tumor were removed Sept. 23, 1926. At this time it was noted that the tumor had not grown and that the volar wound had healed well. The pain and tingling had practically disappeared in the interval. No further trouble had been experienced in the hand, except at one time when after a 10 day's work, the hand had swollen causing pain. The swelling soon went down.

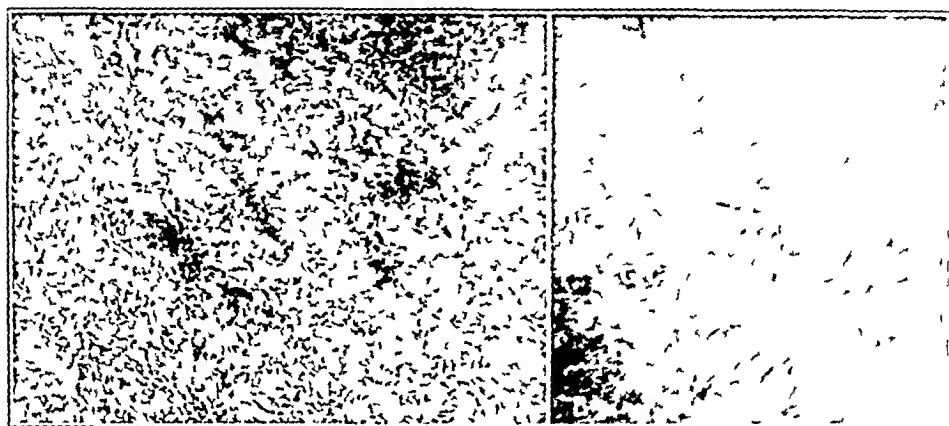


Fig. 8—*A* (case 6). A mass of foamy cells (*FC*) was seen lying in an area of endothelial cells. Many were isolated, others lay in larger groups. They gave the appearance of degenerative changes. *B* (case 8). A smaller mass of foamy cells, *FC*, lying in a fibroblastic area. A giant cell (*GC*) is shown here. The foamy cells appeared to be a degeneration and suggested that a later stage will be the formation of cholesterol clefts as shown in figure 10.

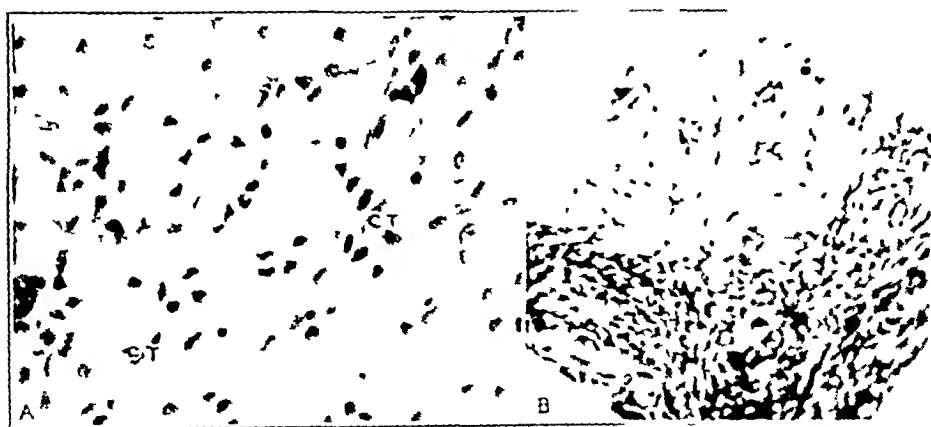


Fig. 9—*A* (case 6). A mass of foamy cells (*FC*) with an eccentric arrangement of their nuclei and a foamy, vacuolar character of the cytoplasm. The cells (*FC*) formed a supportive structure for the foamy cells. *FC* was seen lying in an area of endothelial cells. *B* (case 8). Many newly formed cells in the tissue area.

however, and there was no further trouble. The mass on the dorsum was nodular and smooth and not attached to the skin. The movements of the tendons could not be felt through the tumor, and the tumor did not move with the tendons. The urine and blood count were normal, and the blood sugar was 0.09 per cent. Two determinations of the blood cholesterol were made, using the method of Bloor, with a cholesterol standard. At one time a value of 165 mg, and at another a value of 143 mg, per hundred cubic centimeters of whole blood were obtained. The roentgen ray showed some involvement of the carpal bones.



Fig 10—*A* (case 6) A small isolated group of foamy cells, *FC*, lying in the midst of an endothelial cell group, *EC*. Some large mononuclear phagocytes, *MP*, were noted. *B* (case 3) Another small isolated group of foamy cells, *FC*, in a rather hyalinized area, some endothelial cells, *EC*, and large mononuclear phagocytes, *MP*, were also seen. *C* (case 3) Cholesterol clefts, *CC* in rather dense scarlike tissue.



Fig 11—Various giant cells from the tumors (figs 4 and 6 show others). *A* (case 2) Some of these giant cells were darkly stained and had dark elongated nuclei; others were lightly stained, and the nuclei were oval and showed a definite nucleolus. *B* (case 3) Here the giant cells had attained enormous size and lay in a clear space, probably an artefact. *C* (case 3) A large foamy giant cell such as Spiess described, the body of the cell filled with cholesterol vacuoles and other foreign detritus.

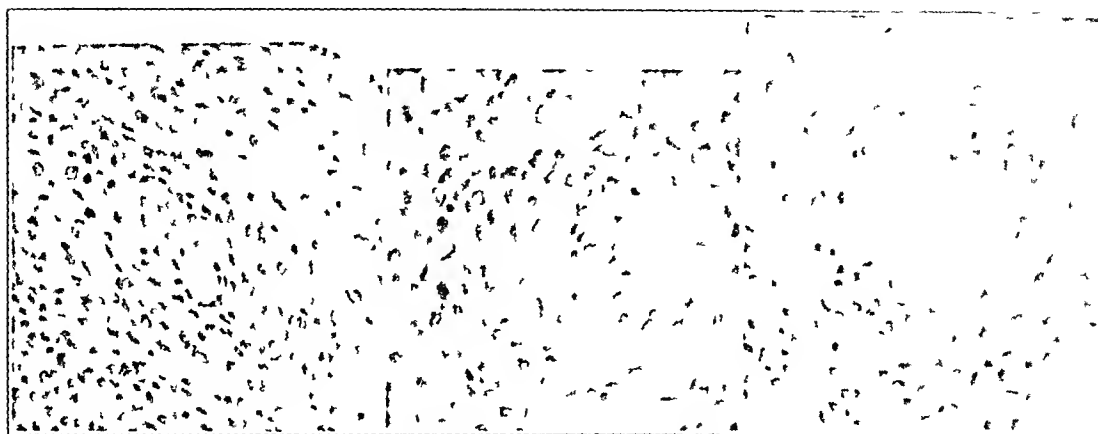


Fig. 12—*A, B* and *C* (case 6). These photomicrographs show some of the recurring figures, present in most of our tumors. The endothelium of the capillaries, as in *A*, was thick and swollen and was taken to indicate proliferative changes, which could be borne out in *B* and *C*. Similar capillary changes are seen, however, in inflammatory tissue. The surrounding cells are endothelial cells, large mononuclear phagocytes and foamy cells.

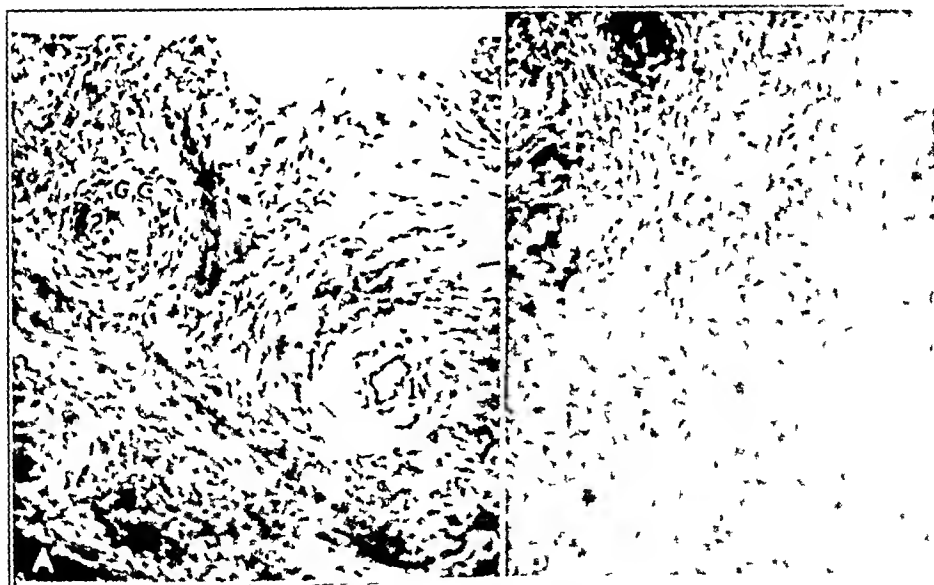


Fig. 13—*A* and *B* (case 7). Other types of changes are seen. In vessel 1 the endothelium is thick and foamy. In vessel 2 the proliferative changes are more progressed and a giant cell (arrow) is seen. The surrounding tissue in which there appeared to be no change.

At operation the tumor was found to involve not only the tendon sheaths, but the joint capsule of the carpus as well. The dorsal tendons were surrounded, but not involved, their tendon sheaths had been replaced by the tumor tissue. As at the previous operation, the tumor was a mixture of yellow and dark red, in spots not unlike a giant cell tumor of the bone. The carpal bones were honey-combed and were curetted out. The triquetrum was removed.

Microscopically the tissue from the joint and tendon sheaths were much alike, except that xanthoma cells were rare in the tumor of the joint. The tumor was a great deal like the volar tumor removed seven months before, the sinuses (fig 15 *A* and *B*) had become more prominent, and the eosinophilic infiltration had disappeared. The bone removed had been invaded, and a few tumor cells were seen in its medullary cavity (fig 16 *A* and *B*). The osteoclastic activity of the tumor was not marked, and there was no evidence of osteoplasia, the impression gained was that the invasion was one of pressure rather than true neoplastic invasion. Few giant cells were seen in any part of the tumor, and not many were seen about the invaded bone.

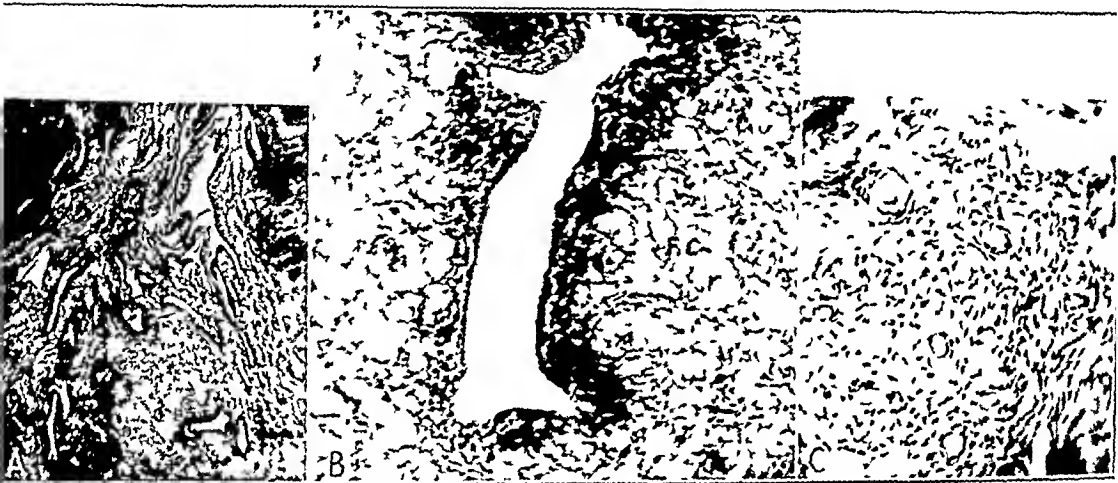


Fig 14—*A* (case 7) A xanthomatic area which contains numerous endothelial lined sinuses, giving the appearance of an angioma. These sinuses lay among xanthoma cells, and it appeared to us that the endothelial cells were gradually taking up cholesterol with the eventual production of xanthoma cells. *B* (case 7) A sinus under larger magnification, *FC*, foamy cells. *C* (case 1) A group of small capillaries such as one might expect in granulation tissue.

CASE 7—Mrs. G., aged 42, was operated on in May, 1926, for a tumor on the ulnar side of the middle finger of the right hand (fig 3). The tumor had been present for two years, having arisen from an unknown cause. It had shown slow but steady growth from its onset, but had caused no pain or discomfort and had given her trouble only when drawing on her gloves and from the fear that it might be malignant. On examination two nodular masses were felt under the skin on the volar and dorsal surfaces of the finger, they were somewhat elongated, and the one on the flexor surface was the larger. They were freely movable under the skin, but seemed to be attached in the depths. At operation they presented the peculiar reddish and yellow coloration typical of the xanthoma with the yellow predominating. The volar tumor was attached to the fibrous tissue about the first interphalangeal joint. The lateral digital nerve ran through it in

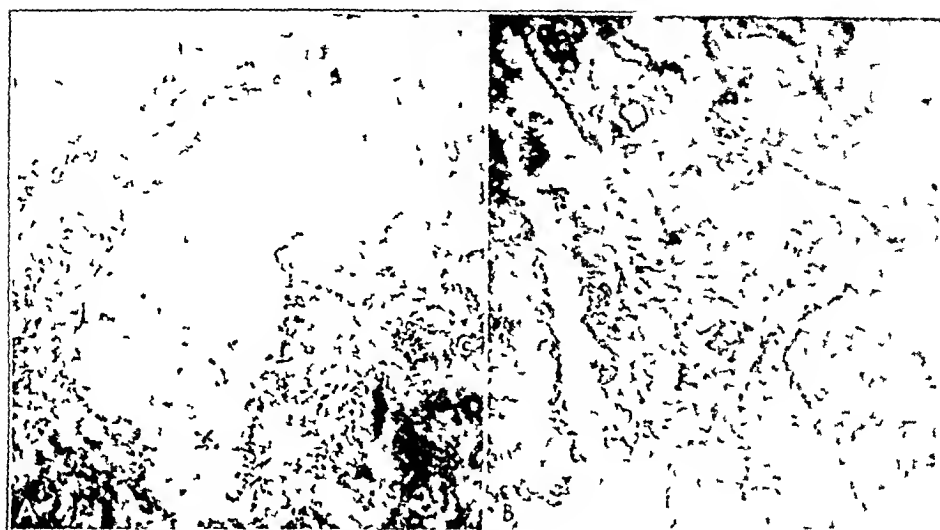


Fig. 15—*A* and *B* (case 6), showing large sinus-like areas similar to those in figure 14 here filled with a conglutina and many white cells. The tumor was vascular, and areas of round cell infiltration were frequent. *Ac*



Fig. 16—(Case 6). In this slide was seen the blood vessel through which the tumor invaded the bone, and the bone was irregularly resorbed. The tumor cells were in the bone. Giant cells were present. The lining of the blood vessel was composed of endothelial cells. The bone was resorbed.

a groove on the surface. The tendon sheath was not involved. The tumor on the dorsum was rather firmly attached to the fibrous tissues about the dorsal tendons. Microscopic section (figs 5 *A*, 13 *A* and *B* and 14 *A* and *B*) revealed a typical xanthoma. A fibrous capsule of adult connective tissue sent down strands of fibrous tissue into the tumor, which disappeared as the deeper parts of the tumor were reached. Xanthoma cells (fig 14 *A* and *B*) were abundant in some sections, not so abundant in others. Endothelial cells were frequent and could be seen to give rise to foamy cells. Blood vessels were numerous and showed proliferative changes (fig 13 *A* and *B*). In the foamy cell areas sinuses were present, some of which were empty, others were filled with blood and some with debris. Pigment, positive for iron, was plentiful, both intracellular and extracellular. No recent hemorrhages were seen.

A blood cholesterol determination made on this patient gave a value of 185.3 mg per hundred cubic centimeters of whole blood. The tumor has not recurred to date.

CASE 8—Mrs. C. G., aged 26, a housewife, operated on in February 1927, had noted a small growth on the right thumb about a year before. She disclaimed any knowledge of a causative factor. Since the onset the growth had slowly enlarged, but it had never given her any real pain or other trouble. She said that it seemed to be tender at times, and that pressure on it nauseated her. The movements of the thumb were not interfered with. The swelling had never opened and discharged. No other similar swelling was present.

Physical examination showed a small, grape-sized, firm mass on the dorsolateral aspect of the right thumb, movable under the skin and not attached to the underlying tissues. It was diagnosed as a benign connective tissue tumor.

At operation an irregular, lobulated, almond-shaped tumor was removed, which looked like suprarenal tissue.

Microscopic section (fig 4 *B*) showed the elements of a typical xanthoma. A connective tissue capsule covered one side of the tumor and sent down into it strands of tissue which gave it a lobulated appearance. Over this capsule there was some loose connective tissue in which areas of hemorrhage were seen. Xanthoma cells were rather numerous and lay in irregular groups. Endothelial cells were present and showed the gradual vacuolization with the final production of the foamy cells. Many foreign body giant cells were present. Blood vessels were not especially numerous; in spots one could see round cell infiltration about them. Pigment and sinuses were not noted.

COMMENT

Table 1 gives in summary the information concerning our eight cases. It is seen that two patients were men and six were women, with two exceptions, all were in the fourth and fifth decades of life. The right hand is most frequently affected. One tumor occurred on the wrist and the rest on the fingers. The duration varied from ten months in case 3 to nine years in case 6. Trauma seems to play a rather important rôle in our series—in three cases severe trauma, in two, recurrent trauma. Pathologically, all the tumors contained giant cells, some in great abundance, others in smaller numbers. Xanthoma cells were present in all but one. Cholesterol determinations were made in three cases, in none of them was there an increase in the blood cholesterol. There have been no recurrences to date in any case, however in

case 8 the interval since operation is too short to be significant. The average time since operation for the others is four and one-half years. The treatment instituted was local excision in all but one case. In case 2 the finger was amputated after a frozen section showed the condition to be giant-cell sarcoma. The tumors were all of moderate size, varying from that of a hazelnut to that of an almond except the one in case 8 which was large and was diagnosed as tuberculous tenosynovitis.

TABLE 1—Data of Light Cases Reported*

Patient	Age	Location	Duration	Treatment	Result
1 Mrs. D. February, 1919	54	Left fifth finger	4 years	Local excision	Healed
2 Mrs. W. September, 1920	53	Right third finger	1½ year	Amputation by saw-bone machine	Healed
3 Mr. R. February, 1921	50-60	Right second finger	10 months	Growth of tumor	Healed
4 Mrs. W. October, 1921	50-60	Finger	7 years	0	Healed
5 Dr. S. July, 1924	31	Right palm	1 year	Aspiration and extraction of contents	Healed
6 M. A. February, September 1926	11	Right wrist	9 years	Local excision with	Healed
7 Mrs. G. May 1926	42	Right third finger	2 years	0	Healed
8 Mrs. C. G. February 1927	26	Right thumb	1½ years	0	Healed

*Cholesterol determinations (normal from 110 to 170 mg. per 100 cc.)

Case 1 96 mg. per 100 cc.

Case 2 98 mg. per 100 cc.

Case 3 111 mg. per 100 cc.

Case 4 115 mg. per 100 cc.

Case 5 141 mg. per 100 cc.

Case 6 185 mg. per 100 cc.

Method: Meyer with modification of procedure.

Method: Meyer with cholesterol crystals.

Method: Floor with cholesterol crystals.

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Method: Floor with cholesterol crystals.

Reurrences: none to date

Average time since operation: 4 years

Longest time since operation: 11 years

Shortest time since operation: 10 months

(Case 8 excluded)

Treatment: Local excision in all but case 2

Case 2: amputation of finger after frozen section

giant-cell sarcoma

*Feature to be noted in the pathology of the tumors is the duration of the tumor in cases 1 and 2. The average duration of the normal cholesterol figures in case 1 is 4 years and in case 2 is 11 years. Treatment in all cases consisted of local excision except in case 2, giant-cell sarcoma of finger.

We have collected from the literature 16 cases of xanthoma tumors of the tendon sheaths and nodules as well as some of them with complete osteoarthritic changes. Case 2 gives the authors no idea of the number of cases reported but claim that this is a complete list of all cases reported that it is sufficiently large to warrant a conclusion.

Discussion—The xanthoma of the tendon sheaths is no longer a rare disease. It is a disease of the tendon sheaths and frequently its true nature is overlooked.

Of 122 cases in which the sex is recorded the women outnumber the men by 68 to 54, a proportion of about 55 per cent women to 45 per cent men, certainly not a decisive figure. Age also plays some rôle the condition usually occurring in adult life. No age, however, is immune. Paviot and Albertin reported a case in a boy, aged 9, Menciére reported one in a girl of the same age, and Garrett reported that one of his cases of fibroma of the tendon sheath appeared at the age of 5. Reverdin saw such a tumor in a woman of 83, and Fritsch reported one in a man of 73. In one of Fritsch's cases the tumor had been present since birth. The average age in the 122 cases is 35 for the women and 39.9 years for the men. Broders gave 47.2 years as the average age for his patients, and ours also seem to be somewhat older.

TABLE 2—*Sources of Reported Cases of Giant Cell Xanthomatic Tumors*

Name	Date	No of Cases	Name	Date	No of Cases
Broca	1860	1	Bellamy	1901	5
Czerny	1869	1	Heller	1902	4
Piquet	1878	1	Martin	1902	1
Gross	1878	1	Malpert and Morichau Beau		
Dennuce	1885	1	chant	1905	1
Reverdin	1885	1	Coenen	1905	6
Mayer	1886	1	Bazy	1907	1
Libougle and Crissier	1890	1	Gaudin	1908	1
Heurtaux	1891	3	Fritsch	1908	2
Reboul	1892	1	Lenz and Abetti	1909	7
Pillet	1893	1	Russel	1911	1
Pillet and Mouchure	1894	1	Hedinger	1912	4
Longuet and Landel	1895	1	Beckman	1915	3
Malherbe	1896	2	Stewart and Flint	1915	2
Bonhomme	1897	1	Pybus	1917	1
Bonjour	1897	1	Ely	1918	1
Wagner	1897	1	Broders	1919	17
Targett	1897	2	Kaufmann	1922	3
Venot	1898	1	Seyler	1922	8
Dor	1898	1	Burton	1923	2
Menciére	1898	1	Garrett	1923	30
Albertin and Paviot	1899	1	Dyke	1924	2
Arcoleo	1899	1	Weber	1924	1
Delbance	1900	1	Miller	1924	1
Mueller	1901	6	Harbitz	1925	7
Tomaselli	1901	1			

Duration—The duration of the growth seems to be of no particular importance except to emphasize its benign character. The average duration in eighty cases was 4.3 years, Broders gave 7.6 years as the average in his seventeen cases. Some had been present from eighteen to twenty years before they were removed, and in the case reported by Fritsch, the tumor had been present since birth and was removed at the age of 31. The tumor in one of our cases had been present for nine years. The duration of the growth does not seem to bear any particular relation to the size. A tumor of from one to two years' duration may attain in that time the size of a walnut or of a hen's egg, while one of many years' duration may be no larger than a cherry.

Trauma seems to be an important factor in many instances. Dennuce's tumor was ascribed to a blow. One of Heller's patients was a

corner and the growth was attributed to his occupation. One of Fleissig's patients was a seamstress, and the tumor occurred on the left hand at the point where the needle was accustomed to prick after being stuck through the cloth. Another of his patients stuck the finger with a fork and the tumor developed at this point. Beckman reported a case in which the tumor was thought to follow some injury at golf. Stewart and Flint record an instance in which the tumor developed after a fall. Elv records one after repeated falls on the ankle. Broders reports a history of trauma in six and of infection in two of his seventeen cases. Delbance's patient was neurotic and rubbed his thumb against his teeth, and the tumor developed at this place. Of our patients, five had a history of trauma—a rather high percentage. It seems to us that trauma may play a role and that it is present more often than the statistics show, and we are inclined to agree with Broders and Garrett that it is an important factor.

TABLE 3—Age and Sex Distribution and Incidence of Trauma in 122 Cases of Xanthoma

	Sex men 54, women 68		Female	Male
Age				
0 to 10			1	1
11 to 20			8	5
21 to 30			18	8
31 to 40			9	9
41 to 50			7	7
51 to 60			6	8
61 to 70			3	4
71 to 80			0	1
81 to 90			1	0
Average age females 35 males, 29.9 Youngest, 5 years, oldest, 83 years				
Average duration in 80 cases 13 years (Broders 7.6 years)				
Longest duration 31 years				
Shortest duration 6 weeks				
Trauma 10% Garrett, 30% probably Broders, 30%, personal, 60%				

As to occupation, there is no agreement, some authors think that laborers are more frequently affected, though this has not been definitely shown.

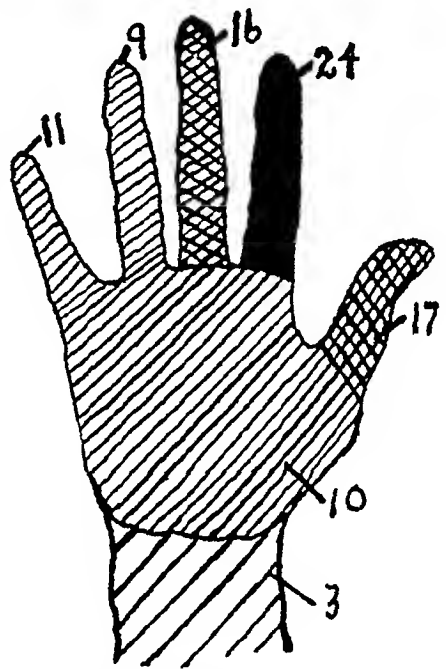
Table 4 shows that in 123 collected cases, ninety-six tumors occurred on the upper extremity and twenty-seven on the lower. Of the ninety-six on the arm, fifty-eight were on the right and twenty-eight on the left hand, while in ten cases this distinction was not reported. The incidence for the separate fingers is shown in the diagram. Of ninety tumors, twenty-four were on the index finger, seventeen on the thumb, sixteen on the middle finger, eleven on the little finger, ten on the palm, nine on the ring finger and three on the wrist. Of seventy-four tumors, fifty-nine were on the flexor surface, ten on the extensor surface and five on both flexor and extensor surfaces. On the lower extremity the right is also the most frequently affected, and here the region of the

malleoli, especially the external, is more often the site of the tumor. It appears to us that the fact that the tumor appears more often on the hand, and on the fingers of the right hand, and on the fingers of this hand that are most subject to trauma, certainly indicates that trauma is a factor in its growth.

The question of hypercholesterinemia in the xanthomas has been especially emphasized since the work of Kawamura and of Pinkus and Pick demonstrated that this was the substance that filled the foamy cells and that in many cases in which there were such tumors there was an increase of this constituent of the blood. In many instances of xanthoma

TABLE 4—Location of the Giant Cell Xanthomatic Tumors*

Upper Extremity, 96	Right, 58	Left, 28	?, 10
Wrist	1	2	0
Palm	8	2	0
Thumb	10	4	3
Index	15	8	1
Middle	11	5	0
Ring	7	2	0
Little	5	4	2
Finger	1	0	3
Forearm	0	1	0
Over ulnar nerve	0	0	1
Surface (74 cases)	Flexor 59	Extensor 10	Both 5
Lower Extremity, 27	Right, 14	Left, 4	?, 9
Ankle	8	0	4
Great toe	0	0	0
Second toe	2	0	0
Third toe	1	1	0
Fourth toe	0	0	0
Fifth toe	0	1	0
Foot	2	0	2
Leg	1	0	3
Thigh	0	2	0



* The upper extremity is by far the most frequent site for these tumors and especially the right hand. The frequency of the separate fingers is shown in the diagram.

multiplex, lesions are found in the tendon sheaths that are similar to the isolated tumors and from this it has been argued by many that the isolated tumors are also associated with an increase in the blood cholesterol. The evidence is, we think, only inferential and is not supported by direct proof. Certainly in those of our cases in which cholesterol determinations were made, no such increase of the blood cholesterol was found. Some instances of xanthoma multiplex are reported in which high blood cholesterol was not present (Rosenthal and Braunisch, 1921). We are not inclined to look on the isolated tumors as being associated with hypercholesterinemia.

The ideas concerning these yellow tumors have undergone many changes since attention was first directed to them by Rayet and Lebert. Following the lead of Nelaton, most of the early authors classed them with tumors arising from bone marrow and assumed that they arose either directly from medullary substance or from misplaced bits of bone marrow substance. Paget described these tumors, and although he notes that they may come from many other than osseous tissues, he does not seem to doubt that myeloma is the correct name for them. Czerny, who likened the tumor he described to an epulis, thought, however, that the tumor might arise from connective tissue and that the wandering cells might play an important role. Gross also seconds many pathologists of his time in the opinion that these tumors are not of osseous origin and that the giant cells may easily arise from the soft tissues as well as from bone. It is hardly a moot point at present, it has been well established that in the vast majority of cases giant cells are probably the response of the organism to foreign material or to certain types of infections and that their presence usually means this and nothing more.

The moot points at present concern the question of the neoplastic or inflammatory nature of the growth and the relation of the isolated growths to increased blood cholesterol. Dor, in 1898, noted the presence of the giant cells in the xanthomatous tumors and the presence of xanthoma cells in the myelomas, and stated that "*il existe un état morbide local identique capable d'engendrer suivant des tissus tantôt des myelomes, tantôt des xanthomes, et quelquefois des myelo-xanthomes*". He thought the tumor was inflammatory in origin and was about the first to suggest such an origin for it. Although the majority of writers before and after him have assumed that the tumor is sarcoma, his views are gaining ground, and, considering the clinical course along with a rather puzzling type of pathologic picture, one is surely justified in assuming that it is not sarcomatous. If the growth is a sarcoma, it is by definition malignant, and if it is not malignant, it cannot be a sarcoma. The medical profession seems to be in the same predicament about this growth as it was about the giant cell tumors of the bone a few years ago. It is pretty well agreed that these tumors are not malignant. Any one who has studied the histories of a series of these cases must agree that the growths are benign, even though they may resemble histologically certain malignant growths. Whether one should accept the opinion of Dor, Fleissig, Broders, Seyler and others and assume that they are inflammatory (Seyler favors calling them granulation tissue tumors) is a difficult point to answer. If not, then one may assume with Levy that they are benign tumors of the reticulo-endothelial system, i. e., histiocytomas. Certainly there is nothing in the growths that is not compatible with granulation tissue, and although the picture is not that

usually seen in granulation tissue all the elements present may be found in granulation tissue, and the assumption may not be so far wrong. We are rather inclined to look on these tumors as inflammatory and not neoplastic.

Gross Pathology—The size to which the tumors may grow does not bear any relation to their age. They are somewhat larger on the ankle than on the hand and larger on the wrist than on the fingers. Most of them are about the size of a hazelnut or walnut, although many have been described as much larger, they have been reported as large as a goose egg on the thumb, the size of a hen's egg on the palm and the size of a pigeon's egg on the middle finger. One in our series which was thought to be tuberculous would have filled a 6 ounce bottle.

Site of Origin—Not all of these tumors take their origin from the tendon sheaths, although they are usually accredited to this tissue. Garrett, in studying 196 tumors of a rather common pathologic make-up, found 135 of the same type, that is, they belonged to the xanthoma group. When these tumors are on the hands or feet they most often come from the tendon sheaths, but even here many take their origin from subcutaneous tissue or other fibrous tissue. Some tumors of the joints have the same pathologic picture as xanthomas of the tendon sheath. Gross, Ferie and Targett reported instances in which the tumor arose from the palmar fascia. In the cases reported by Stewart and Flint, one had taken its origin apparently from the volar carpal ligament. Longuet and Landel reported a tumor coming from the fibrous capsule of the talocalcaneal joint. In one of Broders' cases, the tumor had taken its origin from the fascia of the leg. Coiten's tumor had come from the subcutaneous tissues of the thigh (not from the fascia lata). In a case reported by Seyler (1922), the tumor had grown about the ulnar nerve, which was easily shelled out from it. It had probably come from the perineurium. In some instances the tumor seems to have had an osseous origin, or at least tumors of similar type some from the bone (Dyke, Ely).

In our cases, the tumor came from the tendon sheath twice, from the palmar fascia once, from subcutaneous tissues three times and from fibrous tissue about joint or bone twice.

Color—The tumors are frequently compared grossly to suprarenal tissue. They present a variable mixture of yellow and brownish red in a gray connective tissue capsule that often sends down into the tumor strands of fibers which divide the tumor into lobules giving it the appearance of marble. The reddish elements are due to the presence of blood or blood pigments in the tumor, following the frequent hemorrhages which are characteristic for the growth. The pigment gives the Berlin Blue reaction for iron. The yellow comes from carotin and

xanthophyll (as E. M. Miller suggested), and not from cholesterol, as is commonly supposed, since cholesterol is colorless. The typical coloration may be entirely lacking, and still the growth may be indistinguishable from other xanthomatic tumors, on the other hand all tumors with this peculiar coloration are not necessarily xanthomas.

Consistency—The tumors are tough and elastic, cut across like fibromas and the hardness combined with the color is enough, according to Bloodgood, to make the gross diagnosis. They vary in their consistency some are hard, as was one reported by Beekman which had the consistency of a cartilaginous tumor. Some contain so much iron that they have to be treated with oxalic acid before they can be sectioned. Others are soft and may feel like lipomas. In one of our tumors the consistency resembled that of a giant cell tumor of bone.

On section they present a capsule of varying thickness, which sends trabeculae down into the tissue, dividing it into lobules of mixed reddish brown, yellow and gray. Blood vessels may or may not be numerous, and the lobule may or may not project above the surface of the cut section.

They are smooth and rounded, usually lobulated, consisting of one large lobule with several smaller ones from its surface. The tumor is frequently composed of a number of separate lobules held together by threads of connective tissue. They are more often elliptical than spherical, spreading out along the side of the finger.

Microscopic Picture—In describing the minute picture of these tumors, we find that they are a great deal like the facetious definition of exophthalmic goiter, which is characterized by neither exophthalmos nor goiter, for these tumors may lack either giant cells or xanthoma cells, but they always possess one or the other, and in the great majority of cases both types are present. They seem to be a clinicopathologic entity rather than a pure pathologic entity. The description may be divided into descriptions of the capsule, the stroma, cellular elements, vascular elements and pigment. The possibility remains that one is dealing not with one tumor, but with several having many things in common.

The great diversity of cellular elements is then most striking characteristic. This has led to a great deal of trouble in their classification. They usually possess a connective tissue capsule (fig 4 A) which sends down fibrous septums into the tumor (fig 6 A), dividing it into lobules (figs 6 A and 5 B and C). These septums are frequently made up of adult connective tissue, not infrequently of fibroblasts (fig 4 C) at other times they become hyaline and contain few or no cells (fig 5 B). At times the septums are absent or scarce, and the tumor is cellular, at other times they may be so numerous and so well developed

that the growth takes on the appearance of an alveolar sarcoma (fig 5 C). The tumor may be cellular in one part without any septums, while in other places it is distinctly alveolar.

The most frequently described cell is a spindle cell (fig 5 A), and many authors have given the name of spindle cell sarcoma to the growth. Paget described the cell in his early description, as did Paquet, Heurtaux, Targett, Coenen, Gaudiani, Pybus, Ely, Kirch, Seyler, Gallett, Levy and many others. We found it in all of our tumors, frequently in great abundance, suggesting sarcoma (fig 5 A). Apparently, a great many of these cells are fibroblasts which result from connective tissue proliferation and are certainly not sarcomatous.

Endothelial cells are found usually in large numbers. They have a reticular cytoplasm (fig 6 B) and show evidence of developing into foamy cells. They are especially abundant in tumors which show evidence of vascular proliferation, and it seems that at times we can trace the cells from the endothelial lining of blood vessels (fig 12 A, B and C). They may also come from other cellular elements of the reticulo-endothelial system. They are frequently filled with pigment when it is present in the tumor (fig 7 B). The same may be said for the spindle cells, which may also take up pigment, showing them to be capable of phagocytosis. Both these cells (endothelial and spindle) may well be inflammatory in nature.

Various other cellular elements are described in these tumors. Perivascular round cell infiltration (figs 7 A and 15 A) is not infrequent and was seen in nearly all our tumors, although this is usually not a marked feature. It may not be present in all parts of the growth, but only in a few places. Polymorphonuclear leukocytes were noted in rare instances, at one time, in the first tumors removed from Mother A. There was a general infiltration of the tumor with eosinophils. At the second operation they were again sought, this time in vain. Other types of polymorphonuclears were infrequently seen, never in any abundance. In the sinuses that will be described later, leukocytes were seen in a higher percentage than one would normally expect (fig 15 A and B). Other infiltrating cells present include large mononuclears, with oval or bean-shaped nuclei many times full of pigment (fig 10 A and B). They belong to the reticulo-endothelial system, having to do with the resorption of the products of red cell destruction or the removal of other products of cellular degeneration. Red blood cells are often seen in the tissues, sometimes perivascular, at other times only the masses of pigment remain to show where a small hemorrhage has occurred. These collections of red cells were numerous in some tumors, in others they were rare, in some tumors the hemorrhages could be found only at the junction of the capsule and the tumor proper.

The foamy cells and the giant cells are the most striking components of the tumors, but they are not present in all of them. In our series the foamy cells were seen in all but one tumor, and giant cells were seen in all of them, in one, however, they were so rare that they were almost missed. The foamy cells (figs 8 *A* and *B*, 9 *A* and *B*, 10 *A* and *B* and 14 *B*) are large polyhedral cells with small pyknotic nuclei which may often be multiple (from two to three to a cell). The cytoplasm is vesiculated, the vesicles being nearly all the same size and separated from each other by granular cytoplasm. The cells are separated from each other by a sort of connective tissue reticulum in which connective tissue nuclei are seen. On staining with sudan III the cells are seen to be filled with a fatty substance which with osmic acid stains gray and shows itself to be a lipid. With polarized light the vesicles of the foamy cells are seen to contain a doubly refractive substance that may be proved chemically to be cholesterol. The foamy cells are present in groups of a few cells (fig 10 *A* and *B*) or as large masses which form a considerable part of the tumor. In other instances the foamy cells may occur as isolated groups of eight or ten cells, not often as single cells. When they are present as large masses they may be distinct from the rest of the tumor (fig 9 *B*). At first glance one might be inclined to think that they were definitely separated from the rest of the tumor, on closer inspection one can see that the boundary is nothing more or less than the simple juxtaposition of the two cellular fields with no tissues between, and that even where the line seems to be distinct the gradual vesiculation of the neighboring cells and the formation of foamy cells from them may be seen. The foamy cells can be traced from both the endothelial cells and the fibroblasts, and may be confined to the periphery of the tumor, or they may occur in all parts of the tumor. In the case of Mother A, no foamy cells were seen in the tumor removed from the cavity of the joint, but some were found in the tumor which had invaded the carpal bones. In the tumor in case 4, none was seen, though the giant cells were abundant. In one case in which the foamy cells were not especially abundant, several foamy giant cells were seen (fig 11 *C*). The significance of the foamy cells is a moot question. It has been well established that they contain cholesterol, which causes their foamy appearance, but just why they should appear in this type of tumor is not known. The suggestion that there has been an increased blood cholesterol is not proved, and it must be assumed that the cells are taking up cholesterol formed as a result of the tissue degeneration. It seems likely that any cell taking up cholesterol will assume the foamy shape and that this is the only significance of these cells. It seems to us that they are most frequently derived from the endothelial cells, many

stages of gradation from the endothelial cells can be seen. In other instances they are derived from fibroblasts.

The giant cells are the next prominent type found in the tumor (figs 4 *A*, *B* and *C*, 6 *A* and *B* and 11 *A*, *B* and *C*). They were seen in all of our tumors, their number, however, being variable. In some of the tumors they were as numerous as similar cells in giant cell tumors of bones, in others they were as rare as they were formerly abundant. They were of every conceivable size, shape and nuclear arrangement. Many resemble the Langhans giant cells, many were small and contained only a few nuclei, others were large, assuming enormous size and containing nuclei numbering in the hundreds. The nuclei may be arranged as a peripheral ciclet or as a central ciclet, they may be scattered throughout the whole cell or at one end or bunched up in the center. Many are filled with foreign particles and detritus or contain cholesterol (fig 11 *C*). The giant cells seem to be produced from the fusion of many endothelial cells or to bud off from the endothelial cells of the proliferating vessels, where they may be seen projecting into the lumen (fig 13 *A*). They do not seem to bear any particular relationship to the foamy cells, in fact, few giant cells are seen in the foamy cell groups, and where the giant cells are numerous, the foamy cells are not abundant. The giant cells are not infrequently loaded with pigment, if so, they are smaller than the cells which do not contain any pigment. Foamy giant cells were noted in one tumor (fig 11 *C*). Where giant cells are numerous, they so pack the tissue that one thinks of a giant cell bone growth (fig 4 *A*). In some sections the cells were so arranged as to suggest an alveolar sarcoma (fig 6 *A*). In the case of *Mis G*, their arrangement suggested the location of vessels which had undergone endothelial proliferations, with the resultant formation of giant cells (fig 13 *B*). In the case in which invasion of the bone was seen (fig 16 *A* and *B*), surprisingly few giant cells were found.

The blood vessels of the tumor are also variable (figs 7 *A*, 13 *A* and *B*, 14 *A*, *B* and *C* and 15 *A* and *B*). In many the vessels have extremely thin walls, are numerous and are apparently normal. They may be extraordinarily numerous, or they may be scarce. Two vascular changes are worthy of note, the endothelial proliferation and the presence of sinuses. The histologic picture of endothelial proliferation was given by Bellamy in 1901. The whole general question of the proliferation of the common vascular endothelium has been considered by those studying the reticulo-endothelial system, and there is still lack of agreement among authorities as to whether the endothelium of the ordinary vessels can give rise to phagocytic cells. Mallory and his school believe that the common vascular endothelium may give rise to various cells that wander out into the tissues in response to various

stimuli as infection, foreign bodies, etc. Aschoff and his pupils and Sabin and his followers do not believe that the common vascular endothelium belongs to the reticulo-endothelial system. It seems to us that settlement of this question might be important in the classification of these tumors. The changes interpreted as endothelial proliferation have been noted in many of our cases. At times such changes were numerous, almost every field showed the thickening of the vessel wall, the fattened endothelial cells, the increase in numbers of these cells and the formation of cells which project out into the lumen of the vessels or which seem to grow outward into the surrounding tissues (figs. 12 *A*, *B* and *C* and 13 *A* and *B*).

The presence of sinuses was noted in many of these tumors (figs. 14 *A* and *B* and 15 *A* and *B*). These sinuses, some vascular and some lymphatic, have led many to call the growths angiomata. At times the sinuses are among the foamy cells (fig. 14 *A* and *B*), and at other times in the endothelial cell groups. They may be numerous in some parts of the tumor and missing in others. In the second tumor of Mother A (fig. 15 *A* and *B*) they were plentiful and were filled with blood.

Pigment was present (fig. 7 *B*) in all of our tumors. It was for a large part non-positive, giving the Berlin Blue reaction, and came without doubt from the destruction of the extravasated red cells. The pigment is mainly intracellular, being taken up by the endothelial cells, by fibroblasts, by the giant cells and by certain large mononuclear cells which may be clasmatoocytes. The pigment is not evenly distributed throughout the tumor, but is more abundant in some areas, others being free from it. In some tumors it lies at the periphery under the capsule. In some tumors it had a sort of perivascular arrangement.

As to evidence of malignancy, the question in our minds is settled, not by the pathologic picture alone, but by a consideration of the clinical picture along with it. Most authors (there are a few exceptions) agree that the tumor is benign and that it should not be called a sarcoma. An analogy may be made with the giant cell tumor of the bone, which has many things in common with this tumor. However, there have been some cases of giant cell tumor of the bone which were reported as giving rise to metastases (Kolodny, and Finch and Grieve give literature of additional cases). In two instances malignancy was suggested to us. In one the capsule in certain spots seemed to be invaded by the cells, and in the other the carpal bones were invaded. No other evidence of malignancy was noted, and it may be that in regard to the tumor of the bone the suggestion of Broders' is correct—that the presence of the giant cells, which are bone absorbers, may have led to the destruction of bone, or, as we suggest, the pressure of the tumor on the bone may have led to necrosis. The capsular infiltration is not sufficient. Suffice it to say that no other evidence of malignancy was seen here.

was no lymphatic enlargement, and the course of our patients to date, as well as of all those from the literature, does not indicate malignancy.

Symptoms—The clinical picture of this growth is simple. The onset is insidious, with a small tumor which the patient may or may not attribute to trauma or to infection. It is of slow, insidious growth and on the finger seldom reaches a size over that of a hazelnut. It causes little or no trouble and when on the hand rarely gives rise to pain, on the foot it is frequently associated with pain. Rosenthal says that on the foot the growth is always associated with pain. None of the tumors in our cases were on the foot, but from the literature one does not get the impression that all on the lower extremity caused pain. There may be some functional disturbance from the size of the tumor. They may interfere with putting on gloves, on a dentist's or a surgeon's hand they may cause trouble in the handling of instruments. If low on the finger they may be subject to trauma from a ring. One of our patients, Mother A., complained of tingling and burning in the wrist and fingers. In one of Bellamy's cases the tumor came on two days after sudden causeless pain.

One characteristic that should be emphasized is the tendency to sudden accession of growth which these tumors may show. They may grow along slowly for several years and then start in rapidly to enlarge. In a case of Paquet's in which the tumor had been present for twelve years when operation was performed, it had reached the size of a pea at the end of ten years, it then started to grow, and after two more years had grown to the size of a walnut. A sudden accession in growth does not necessarily mean that the growth is malignant. Trauma may lead to more rapid growth. Ferre's patient said that after starting arms practice the tumor grew more rapidly, and in the case of Pilliet, the tumor, which had been quiescent for many years and which had been present since birth, started in to grow after it had been punctured, with the recovery of some blood. In a case of ours, the tumor began to grow suddenly eight years after the onset. In this same case, after removal of the volar mass, there was a sudden causeless pain with swelling and redness, which, however, subsided later.

One point to be noted on examination is the consistency of the growth, which is about that of a fibroma, elastic and at times tense and pseudofluctuant. It does not have the hardness of an osteoma or of a chondroma. As a rule, the skin is movable over it, and the tumor can be moved over the tendons and bones. Rarely is the skin attached to them, and they ulcerate only if surgical treatment has been applied and infection introduced. Lymphatic involvement never occurs.

Diagnosis—Xanthomas are among the most common tumors of the finger. A solid growth, movable under the skin and attached to the bone, is in a large number of cases a xanthoma. It should be differ-

entiated from the chondroma, which is harder than the xanthoma, from lipoma which is softer, from the carcinoma, which affects the skin, from the osteoma, which is harder and is connected with the bone. A ganglion is smaller and is usually on the extensor surface. Tuberculosis of the tendon sheath may be difficult to differentiate, as was noted in one of our cases, in which the growth was at the wrist on both volar and dorsal surfaces and was thought to be tuberculous before operation. Fibromas of the tendon sheaths occur, but they are rare. Tumors of muscle or of tendons are rare, but should be thought of. Tenosynovitis and tuberculous dactylitis are possibilities. One case reported by Fleissig was considered a paronychia at operation.

Prognosis—Metastases did not occur in any of the cases found in the literature or in any of our cases. No authentic cases of death from a giant cell xanthomatic tumor of the finger have been reported in the literature, so far as we can ascertain. A definite tendency to recurrence has been noted many times by all who have written concerning this tumor. The percentage of recurrence is, however, not high (10 per cent). In the case reported by Gross, the tumor recurred three times in three weeks after operation, but after removal of each growth it finally healed and had not recurred a year after the last operation. In one of Heintau's cases the growth recurred six months after first removal and was locally excised again and remained cured. The tumor in Bonhomme's case recurred. Three of the tumors reported by Targett recurred, but evidently none of the patients died from the growth. In Tomaselli's case the tumor began to grow rapidly two years later, and the foot was amputated. The tumor in Martini's case also recurred, and was removed a second time, the patient was cured. One of Fleissig's patients had a recurrence of a tumor that had been removed three years before. Garriett reported five recurrences in thirty fibromas of the tendon sheath.

Treatment—The treatment of this tumor has become well established. Its resemblance to sarcoma has led many to advise a mutilating operation for a relatively harmless condition, however, and probably many fingers have been sacrificed because of this confusion. Fortunately, it is not a frequent condition. It is well agreed that local excision or enucleation, as in other types of benign growths, such as lipoma or fibroma, is all that is required. Even when it recurs, as it does in a certain percentage of cases, the new growth should again be removed, and the finger or hand should not be amputated. It should be treated usually in the same fashion as giant cell tumors of the bone.

The tumors usually shell out easily and are encapsulated, at least in the early stages, though later the encapsulation is lost. The origin from the tendon sheath is often recognized, and this fact should lead

the surgeon to think of xanthoma at once, as this is by far the most frequent tumor of the tendon sheath. When the growth is removed, the tendon is not infrequently laid bare. The gross appearance of the tumor is also suggestive, and when the origin and consistency are considered, it makes an almost pathognomonic picture. They tend to be the size of hazelnuts and are lobulated on the surface, so that they often appear to be made up of a conglomeration of several lobular masses, at times the fibrous strands from the capsule are seen to divide the surface up into lobules. The same lobulation can be seen on the cut surface, the trabeculae running from the capsule down into the tumor. The tumor is firm, with about the consistency as that of a fibroma. Usually the cut section of the tumor is solid—cysts are rarely found in it. The lobules are of different colors, the most prominent color being yellow, varying from canary to a deep golden shade. The color accounts for the naming of the growths. Mixed in with these yellow nodules are other colored nodules, some of them being a dark red or reddish brown like a giant cell tumor of the bone. These areas on microscopic examination are usually found to contain the giant cells and are often loaded with a Berlin Blue positive pigment originating from blood. The area between the nodules is gray or white and microscopically is found to be connective tissue, young or old. The pigment may lead to misunderstanding, especially on microscopic examination, when it may cause confusion with melanoma.

On frozen section three characteristics should be looked for. The giant cells are of great importance. As Bloodgood remarks, if these are of the foreign body or epulis type, the diagnosis of sarcoma can be practically excluded. Xanthoma cells are also important, as their presence in the tumor excludes sarcoma. The pigment is important, as it gives the positive reaction for iron, and blood cells which give a clue to its origin are frequently found in the tissue. The pigment may lead to an erroneous diagnosis of melanoma, unless the characteristics of its distribution are noted. Instead of regular distribution in the cells it tends to appear in various-sized granules, many of which are as large as the nucleus (Smith, 1924). Some of the pigment is extracellular.

If the tumor recurs, it should be removed a second time, as in cases of giant cell tumor of the bone. Cases are reported in which the tumor has been removed three times, resulting in eventual cure without amputation. Recurrence is almost to be expected, unless great care is exercised in removal, and even then it takes place in a certain number of cases.

CONCLUSIONS

The giant cell xanthomatic tumors of the fingers and hands that occur as isolated growths are benign. They show some tendency to recur if incompletely removed but they do not produce metastases.

Pathologically, they are polymorphic and may be confused with sarcoma, and they often have the appearance of endothelioma or angioma, but there is nothing in them that is not compatible with granulation tissue. We do not believe that there is any increase in the blood cholesterol in the isolated tumors. The right hand and certain fingers of this hand are most frequently affected, and trauma appears to be a frequent cause for the growth. They should be removed locally and do not require a mutilating operation for cure.

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MALIGNANT TUMORS OF THE TESTICLE

WITH SPECIAL REFERENCE TO CLASSIFICATION*

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Invasion of the testicle by neoplastic disease is notably uncommon as compared to its occurrence in other parts of the body, explicitly, malignant tumors of this organ constitute less than 3 per cent of all the malignant growths encountered throughout the human body.

Despite this rarity, however, the unique and unusual features which characterize and distinguish these tumors, both structurally and clinically, have focused on them a degree of interest and study in striking disproportion to their observed incidence and have established their importance in medical literature.

Clinically, this condition is usually conceived of as a solid tumor of the testicle, often static for a considerable period, but eventually presenting characteristics of slow local growth, which is finally expressed as widespread general metastases. Variations from this sequence are not infrequently seen, however. The disease may be met first in the form of metastatic tumors of the brain, lung and abdomen in a young person in whom an apparently innocent testicular tumor, possibly of some duration, has suddenly initiated a process of general dissemination with little or no gross clinical indication of its altered rôle. In other instances, the sudden development of an abdominal or pulmonary tumor may lead for the first time to the discovery, during the course of a routine search for origin, of a testicular mass the benign appearance of which belies the offspring to which it has given birth. Startling and spectacular events of this nature are almost unparalleled in clinical experience and mark this disease as one of the clinician's most dreaded problems.

The structural features of these tumors present a different claim on the interest. From its inception, this phase of the subject has been responsible for a wide diversity of opinion concerning the nature and origin of malignant testicular tumors as well as their relation to embryonal structures of tridermal type found in the testicle.

The interest among pathologists and embryologists in the subject is attested by a voluminous literature, whose development has done much

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to dispel confusion and to standardize nomenclature. Discussion is still alive, however, regarding fundamental details of morphology and histogenesis, although the controversy has finally and definitely resolved itself into two schools of thought, each of which numbers among its adherents recognized eminent authorities and each of which advances important facts in proof of its contention.

Historical reference to the growth and evolution of the present theories throws some light on the underlying problems involved and justifies, in a measure, the irreconcilable difference of opinion which still exists.

The first recorded observation in this field seems to have been made in 1696 by Saint Donat, who described a rudimentary skull as a constituent of a testicular tumor. Subsequently, Proschaska, in 1803, and Perone, in 1833, made similar observations, noting the presence of fully differentiated tissues, such as hair, teeth and bones as elements of these tumors (Ewing). The real significance of these observations was made apparent only in 1856, when Johnson¹ identified in a solid, undifferentiated tumor of the testicle elements of all three primal germ layers in the form of bone, connective tissue and cysts lined by flat, columnar and ciliated epithelium. In 1887, Langhans, carrying on from this point, classified many tumors hitherto called pure carcinoma, alveolar sarcoma, etc., (i. e., unicellular) as of teratoid or teratogenous origin and further proposed that a large proportion of testicular tumors were of this nature. Wilms² made further advance in 1896 by classifying all complex tumors of the testis as teratogenous and by extending this grouping to include many structures previously classed under a varied terminology. He approached some degree of standardization by his classification of these mixed tumors under two heads, viz.

(1) Embryomas, which are large cystic tumors with an intracystic projecting tumor mass made up of fully differentiated tissue approximating the orderly arrangement of fetal rudiments. These tumors, whose tissues are of the adult type, are commonly called dermoids, are extremely rare and are usually of benign character, clinically.

(2) Embryoid tumors or teratomas, which are solid tumors comprising elements of all three primal germ layers, undifferentiated, embryonal and devoid of orderly arrangement.

The first group is of little clinical interest because of its benign character and its extreme rarity. The second group, on the other hand, exhibits structural and clinical features of peculiar interest. It was observed (Wilms,² Pick, Chevessau³) that there was a marked tendency

1 Johnson. Cystic Disease of the Testis in an Infant and Probably Congenital, *Tr. London Path. Soc.* 1: 241, 1856.

2 Wilms. Embryone u. embryoide Tumoren d. Hodens, *Deutsche Ztschr. f. Chir.* 49: 1, 1898.

3 Chevessau. Tumeurs du testicule, *These de Paris* 1906.

on the part of these mixed, undifferentiated tridermal tumors for one element or germ layer derivative to assume aggressive activity and to overgrow or suppress accompanying elements with the eventual production of what appears to be, on casual study, a pure, homologous or monodermal structure. Viewed in this light, many tumors previously regarded as pure, unicellular adenomas or carcinomas presented, on careful search, unmistakable evidence of suppressed elements, thus establishing their original tridermal nature.

Obviously, this conception extended the scope of the tridermal or teratogenous tumors to include many so-called homologous tumors hitherto placed under a variety of nomenclatures, and some authorities were inclined, at this point, to accept this origin for all malignant epithelial tumors of the testicle, regardless of their homologous or heterologous structure.

On the other hand, Chevessau,³ who was among the first to recognize the principle of monodermal predominance in tridermal tumors and who accepted the teratogenous origin of many so-called homologous structures, was more conservative in the application of this principle. There still remained outside of the tridermal group, in his opinion, a large number of testicular tumors (estimated as about one-half) whose cellular morphology suggested another origin and in which no evidence of suppression could ever be detected, i. e., true homologous structures.

This particular tumor, which thereupon assumed a prominent place in the discussion, was described as medullary, cellular and with scant reticulum. The cells themselves were large, round or polyhedral, with large vesicular nuclei and presented, according to Chevessau, a picture identical with that found in the spermatocytes of the spermatogenic cycle. He therefore chose to regard the adult cells of the seminiferous tubules as precursors of these tumors and proposed for them the significant term of "seminome."

This theory of origin of this common and much discussed tumor of the testicle was generally confirmed and accepted by many competent observers subsequently. Thus two main classes of testicular neoplasms were determined, differing essentially in cell morphology and histogenesis: (1) the embryonal, distinguished by their heterologous, atypical structure and embryonal origin and (2) the simple, homologous unicellular growths arising from fully differentiated adult tissues.

As recently as 1921 Schultz and Eisendrath,⁴ in a review of a series of fifteen cases of malignant testicular tumors, classified nine as heterologous or atypical and six as definitely of the seminome type in which no evidence of heterologous tissues could be found. They accept the teratogenous origin of all heterologous tumors and include as well in

4 Schultz and Eisendrath. Histogenesis of Malignant Tumors of the Testis, Arch Surg 2:493 (May) 1921.

this group all atypical adenomatous tumors, even in the absence of demonstrable heterologous elements. On the other hand concerning the seminoma type of tumor they confirm in general the observations of Chevessau regarding the close morphologic resemblance between the cells of these tumors and those of the spermatogenic cycle emphasizing, as further confirmatory evidence of the origin, a variety of nuclear forms observed in the tumors and identical with certain nuclear changes observed in definite stages of spermatogenesis. They consider this evidence ample to establish the origin of these tumors from adult seminal epithelium and in view of their failure to demonstrate the presence of associated heterologous tissues in any single instance to preclude the possibility of teratogenous relationship for these structures.

The stability of this conception of testicular neoplasms, as sponsored by Chevessau and others, is challenged by another school of thought, of which Ewing⁵ is the leading exponent. The latter, in 1911, after making a careful analysis and study of a series of nineteen cases, arrived at conclusions which tended to simplify as well as to revolutionize preexisting ideas. His hypothesis is foreshadowed by a preliminary assertion that "Having seen the gradual inclusion of many apparently unrelated benign and malignant tumors of the testis into the single group of teratoma, suspicion arises that all or practically all testicular tumors may owe their origin to much the same embryonic disturbance."⁶ In short this hypothesis refers to a teratomatous origin not only those frankly mixed, heterologous tumors of the testicle but also homologous or apparently homologous tumors, benign or malignant, epithelial or mesoblastic.

Ewing is unwilling to accept an extrateratogenous origin of the common large-celled tumor, he places it definitely in the same group with the mixed tumors and submits convincing evidence in support of his contention that it represents a one-sided development of a teratoma. He points out that the sole justification for classing this tumor as a pure, homologous form is based on the failure to demonstrate heterologous elements, and that this is a faulty premise because these tumors are admittedly examined after they have become well advanced, when, according to the principle of predominance, ample opportunity has been afforded for complete suppression of slowly growing and scanty elements of the original structure. He therefore believes that failure to find teratogenous elements in a fully developed seminoma is inadequate to disprove its teratogenous origin. Furthermore, regarding the significance attached to the reputed resemblance between the cells of this tumor and spermatogonia as a proof of origin, he recalls the fact that the cells

5 Ewing Teratoma Testis and its Derivatives Surg Gynec Obst **12** 230, 1911

6 Ewing Neoplastic Diseases ed 2 Philadelphia W B Saunders Company, 1922

of the true adenomas of the testicle are quite unlike their precursors, and it is therefore difficult to explain why, in a more malignant carcinoma, the cells should revert to normal type. Finally, as the most convincing indication of the teratogenous relationship of these tumors, he demonstrates in one of his own cases the occurrence of characteristic seminoma structure in combination with frank teratogenous elements.

Ewing therefore concludes that the data submitted do not satisfactorily prove that any considerable proportion of testicular tumors arise from tubules or stroma, on the contrary, he concludes that tumors of this organ belong to the embryonal class and that at least the majority of these embryonal tumors arise from teratomas.

Although this conception has not met with the prompt and general acceptance which its supporting evidence merits, it has at least stimulated a more careful study of the seminoma tumor. But despite the renewed interest, Ewing's observations have met with but scant confirmation, and the majority of writers retain the seminoma in the nonteratogenous classification. In 1923, however, Hinman, Gibson and Kutzman,⁷ in an effort to clarify this disputed point, made a careful review of a series of seminoma tumors and were able to demonstrate, in one of them, mixed tissues of various types associated with the typical seminoma structure. These writers thereupon revised their classification to include the seminoma under the teratogenous grouping, thus corroborating the classification of Ewing. O'Crowley and Martland,⁸ as a result of their study of thirteen cases of testicular tumors, expressed the opinion that for all practical purposes, there exists but one type of tumor of the testicle, viz., teratoma, but they submit no histologic evidence of the teratogenous nature of the seminoma.

Therefore, in view of the fact that the nature and classification of the common malignant tumor of the testicle is still a matter of controversy, I take the liberty of presenting herein, as the basis of this report data derived from a single case of teratoma testis in which the observations appear to offer a worthy contribution to the discussion. The case in question was recently encountered clinically after it had run the conventional course from focal tumor to visceral metastases. Death eventually followed from these visceral deposits. Subsequently careful postmortem studies, gross and microscopic, were carried out and interpreted under the direction of Dr. Paul Klemperer. The clinical and pathologic records follow.

7 Hinman, Gibson and Kutzman. Malignant Tumors of the Testicle. *Ann Surg* **82** 552, 1925, Radical Operation for Teratoma Testis, *Surg Gynec Obst* **37** 429, 1923.

8 O'Crowley and Martland. New Growths of the Testis, *Surg Gynec Obst* **38** 486, 1919.

REPORT OF A CASE

History—A young man, aged 24, was first seen in an acute emergency and gave a history of sudden onset of severe upper abdominal pain. Within twenty-four hours, the pains had become generalized over the abdomen, were colicky in character and were associated with persistent and uncontrollable nausea and vomiting. During the ensuing week, cathartics and enemas had been freely given but without result, the abdomen becoming gradually more distended and the patient progressively weaker and more emaciated owing to inability to retain food.

The patient said that for some months preceding this attack he had suffered from a chronic dry cough and "nervous indigestion." He said that he had never had robust health and that he had always been thin and underweight. He had been operated on by Dr. Oswald S. Lowsley one year before for tumor of the left testicle, following which his health had remained comparatively good until the onset of the present symptoms. This tumor was noticed only one month before operation, but during this interval had slowly increased in size, there was no history of injury. The patient had had mumps at the age of 15. He did not give a history of venereal disease.

Physical Examination—On examination, he appeared pallid, emaciated and evidently acutely ill. The heart was normal, and no signs of a pathologic condition could be detected in the lungs. The abdomen was generally and tensely distended, free fluid could be detected in the flanks, and intestinal peristalsis was plainly visible through the thinned abdominal wall. General tenderness and rigidity precluded the possibility of detecting intra-abdominal masses. Rectal examination disclosed a distended ampulla and Douglas' pouch. The patient was in a desperate condition with rapid, low tension pulse and persistent vomiting of fecal type.

Operation—An immediate operation was advised under diagnosis of intestinal obstruction and was carried out under local anesthesia. In view of the patient's grave condition, a rapid enterostomy was performed through the right lower quadrant incision, utilizing first the presenting loop of distended intestine. Although the enterostomy functioned well, evacuating intestinal contents and gas, the patient failed to respond and died twelve hours after operation.

Autopsy—A summary of the relevant gross pathologic observations follows. In the abdomen an intestinal obstruction was found 15 cm. proximal to the ileocecal valve, at which point the ileum was found intussuscepted into itself, and at the apex of the intussuscepted loop there appeared a pedunculated tumor about the size of a walnut. The left lobe of the liver showed a walnut-sized tumor. A single large retroperitoneal lymphatic gland was noted at the level of the splenic flexure.

The lungs showed numerous tumors scattered throughout the parenchyma, varying in size from that of a cherry stone to that of an apple. On gross section, these appeared to be of two types, some were deep red and hemorrhagic, and some were white or mottled white. All were soft, with the exception of the one in the right upper lobe which was firm, white and cystic. Several large hilum glands compressed the esophagus in the mediastinum. The diagnosis at autopsy was (1) multiple metastatic tumors of both lungs, left lobe of liver, mediastinal and retroperitoneal lymphatics, (2) pedunculated tumor of lower ileum with intussusception and intestinal obstruction.

Microscopic Examination—The pathologic report on the primary testicular tumor removed from the patient one year previously, as obtained from the record through the courtesy of Dr Oswald Lowsley, was as follows

"The specimen consists of a globular mass of tissue measuring approximately 5.5 cm in diameter. It is composed of the epididymis and a tumor of the body of the testicle leaving a crescent of about 1 cm in thickness of



Fig 1—Metastatic focus in lung showing island of cartilage

testicular tissue at one pole. Cut section shows a brownish discolored surface with many cystic cavities filled with a somewhat viscid material. The more solid portions are grayish white and are the seat of irregular hemorrhagic foci. Section shows the picture of a teratogenous tumor with areas showing the characteristics of embryonal adenocarcinoma.

Metastatic Tumors—Sections were obtained for study from the various pulmonary foci as well as from the solitary nodule in the liver, and typical sections

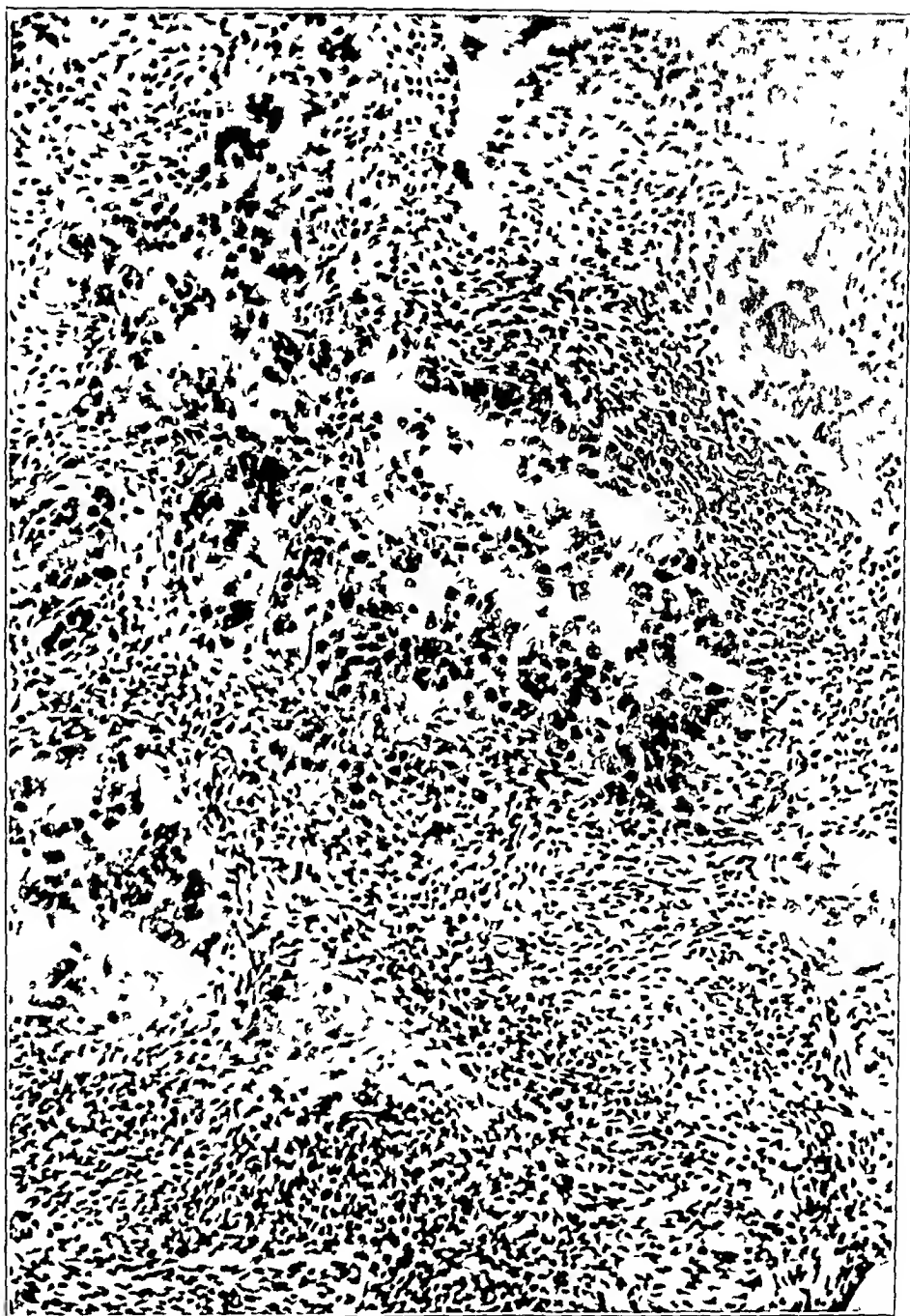


Fig 2—Metastatic focus in lung. Diffuse lymphoid stroma, cyst lined by columnar epithelium, areas of diffuse large round cells with vesicular nuclei.



Fig 3—Metastatic focus in the liver, multinucleated islands of syncytium and the large glycogen-holding cells of Langhans

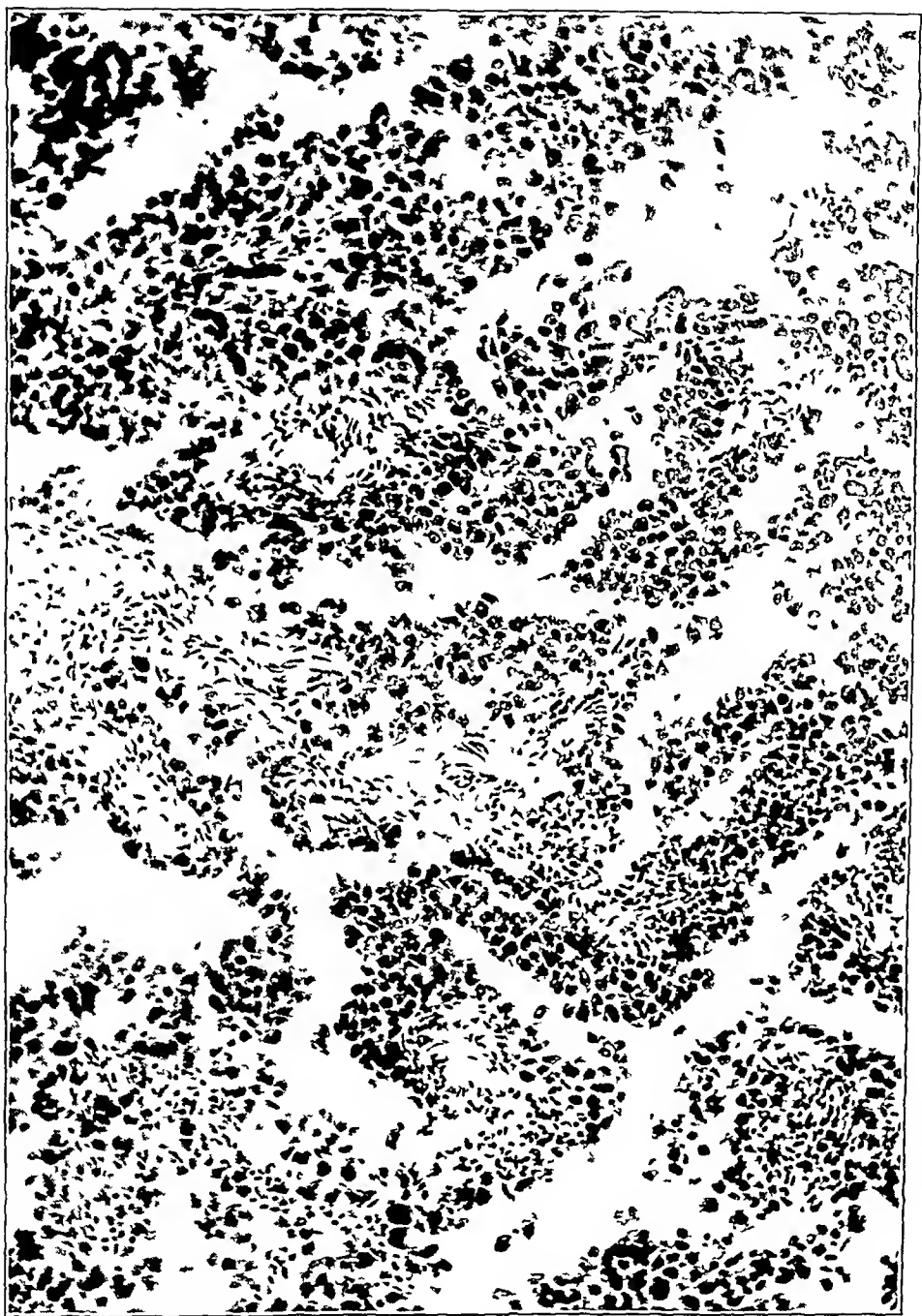


Fig 4—Metastatic focus in the lung Large round-celled tumor with fine lymphoid stroma and with tongue of loose connective tissue seminoma, or embryonal carcinoma

are reproduced in the accompanying figures. From these, it was at once evident that the original focus in the testicle, said to be embryonal adenocarcinoma, had given rise to a variety of deposits in which all three primal germ layers were represented. In figure 1 mesodermal elements in the form of an island of cartilage are the most prominent feature. In figure 2, entoderm and mesoderm are represented respectively by a cyst lined by columnar epithelium and a diffuse lymphoid stroma. Figure 3 pictures the ectodermal derivative, the interesting chorioma⁹ identified by its multinucleated buds of syncytium and its large glycogen-bearing cells of Langhans. Figure 4 is of particular interest and significance for the purposes of the present discussion.

Here may be seen the typical large round cells with large vesicular nuclei. In some areas, the cells are diffusely scattered in solid cords through which runs a faint lymphoid stroma, in others, a more pronounced connective tissue framework appears to form a support for indistinct alveoli. Comparison of this picture with that described and figured as characteristic of the seminoma type of tumor (Chevessau,³ Schultz and Eisendrath¹) shows that they are identical.

COMMENT

To recapitulate, for purposes of interpretation, the case here reported presents clinically the classic sequence of events, i. e., testicular tumor, visceral metastases and death.

Although the entodermal derivative predominates in the primary tumor in the form of embryonal adenocarcinoma, the potentialities of the other suppressed layers are evidenced by a variety of visceral metastases in which all three germ layers are represented. One of these metastatic deposits discloses a structure which has been identified by advocates of Chevessau's theory as characteristic of the seminoma tumor which, because of its cell morphology and its supposed homologous nature, is said to be derived from the adult cells of the seminiferous tubules, thus precluding any teratogenous relationship.

Granted the assumption that figure 4 represents characteristic seminomatous structure, it is evident that this type of tissue appears in a deposit associated with a group of undermal visceral metastases whose origin is unquestioned. Therefore, if it is true, as stated by Schultz and Eisendrath,⁴ that "in any given tumor all the metastases will be formed by the particular tissue components of the primary tumor which has taken on malignant proliferation," it follows logically that at least in this instance seminomatous tissue was a constituent of a mixed heterologous tumor of undoubted embryonal type.

If the foregoing premise is correct, one may predicate thereupon the conclusion that, at least in an isolated case, seminomatous tissue has been

⁹ Cooke. Chorioepithelioma of the Testicle, Bull. Johns Hopkins Hosp. 26: 215, 1915. Frank. Chorioepitheliomatus Proliferation in Teratomata. J. A. M. A. 46: 248 (Jan. 27) 1906.

demonstrated as an element of an heterologous embryonal structure of teratomatous nature

The general conclusion seems justified, therefore, that (1) the large-celled tumor of the testicle is of embryonal type, (2) that the theory of its invariable unicellular or homologous nature is herein disproved and (3) that the evidence adduced from this case substantiates Ewing's theory of its teratomatous origin

BONE IN ARTERIOSCLEROTIC EXTREMITIES *

SYDNEY M CONE, MD

BALTIMORE

In former articles I have stated that bone is modified by circulatory alterations. The changes are progressive, retrogressive or a combination of both, depending on the predominance of passive or active hyperemia. Alternations of active and passive congestion are more influential in upbuilding than the steady continuation of either. I¹ have seen a similar pathologic condition of the ribs in more than 200 cardiovascular cases (fig 1) of long standing. The changes in bone cells and the modification of matrix and marrow were similar to those in the cases I describe here.

Edema, softening of the matrix and enlarging lacunae relieve the bone cell from imprisonment and pressure and allow it to recover vitality. This process is marked at the borders of cancelli, especially in the spongiosa. The activity of these cells is evident in their proliferation to masses of syncytium resembling callus. I have noted this in the proliferation of bone cells in the formation of callus in transplants of bone in muscle. Osteoblasts border old cancelli, and new bone is deposited on them or on branches as new cancelli. Congestion and leakage of red blood cells add to the pabulum. Relieving the pressure allows the cells to unfold their activity in this better medium. The reticulo-endothelial system and capillaries partake of the new stimulation to growth. This is seen in the formation of connective tissue and new vessels in the marrow.

In my cases I saw regressive and progressive tissue changes involving periosteum, bone matrix and marrow without evidence of infection. The pathologic condition must be attributed to a primary circulatory cause analogous to the modification of muscle and soft parts in the experiments of Brooks² and Jepson³. Analogous changes in the liver

* From the Department of Pathology of the University of Maryland.

1 Cone, S. M. Bone Pathology in Relation to General Pathology, *Am J Orthop Surg* 6 607, 1908, A Case of Carcinoma Metastases in Bone from a Primary Tumor of the Prostate, *Bull Johns Hopkins Hosp*, no 86, 1898, The Pathology of Osteitis Deformans, *J Bone & Joint Surg* 4 751, 1922, Activities of Bone Cells, *J Bone & Joint Surg* 7 894, 1925.

2 Brooks, B. Pathologic Changes in Muscle as a Result of Disturbance of Circulation. Experimental Study of Volkmann's Ischaemic Paralysis, *Arch Surg* 5 188 (July) 1922, ext *J A M A* 79 681 (Aug 19) 1922.

3 Jepson, Paul. Ischaemic Contracture, *Ann Surg* 84 785 (Dec) 1926.

and other organs occur in old cardiovascular cases, in which atrophy and fibrosis result

Adam⁴ refers to the formation of bone and soft parts under the influence of passive congestion. He mentions the clubbed fingers in cardiac cases referring to the osteopulmonary atrophy of Marie.

Von Recklinghausen⁵ cites many cases of osteoplasia due to vascular congestion. He compares the hyperplasia of bone in chronic osteitis to elephantiasis due to congestion. He reports a case of exophthalmic goiter with vasomotor involvement and hypertrophy of the bone. He finds vital absorption and hypertrophy in congestion near metastases of cancer and reports overgrowth of bone associated with the venous congestion of varicose veins. Spencer,⁶ Axhausen,⁷ Stilling⁸ and Greig⁹ have likewise noted this association.

Greig states

It is possible that the circulatory disturbances which caused the varicose veins from the calf to the groin might at the same time have altered the nutritional conditions in the bone itself and so affected the vitality of the osteoblasts, altering their function.

Fehr,¹⁰ with Greig and von Recklinghausen, notes the absorption of bone and widened lacunae due to the action of fluids of the blood in hyperemia. He refers to the enlargement and growth of the bone cells in these cases. He quotes Heitzmann (Stricker's "Jahrbucher," 1873), who stated that the changes in blood volume are held in bounds by dense cortical bone, and that a solution is necessary if the volume changes.

Ziegler¹¹ writes

In case the growing properties of the bone cell are not destroyed, the strength of the blood supply may cause new growth of bone. It is possible that the

4 Adam, J. G., and Nichols, A. G. *The Principles of Pathology*, Philadelphia and New York, Lea & Febiger, 1909, vol. 2, p. 1018.

5 Von Recklinghausen. *Die Fibrose oder deformierende Ostitis, die Osteomalacie und die osteoplastische Carcinose in ihren gegenseitigen Beziehungen*. Festschrift zu Rudolf Virchow, 1891.

6 Spencer, W. G. *The General Pathology of Bone*, *Lancet* **1** 1471, 1896.

7 Axhausen, G. *Histologische Studien über die Ursachen und den Ablauf des Knochenumbaus im osteoplastischen Karzinom*, *Virchows Arch f. path. Anat.* **195** 358, 1909.

8 Stilling, H. *Ueber Osteitis Deformans*, *Virchows Arch f. path. Anat.* **119** 542, 1890.

9 Greig, David M. *Osteitis Fibrosa*, *Edinburgh M. J.* **24** 324 (May) 1920.

10 Fehr, M. *Studien über den Bau des Knochens und seines Lebens im gesunden und kranken Zustande*, *Arch. f. klin. Chir.* **17** 19 and 232, 1874.

11 Ziegler, E. *Ueber proliferation Metaplasie und Resorption der Knochengewebe*, *Virchows Arch f. path. Anat.* **73** 355, 1878, *Lehrbuch der speziellen Pathologie*, Jena, 1906.

dissolving of bone salts starts the bone cell activity. Qualitative as well as quantitative modifications of the circulation are necessary for bone changes.

He quotes Cohnheim, who stated that the strength of the blood current influences activity of bone cells in metaplasia.

Wells¹² says

The amount of blood supply is the important factor in determining pathological ossification. With too free a circulation there is no calcification and no ossification with too little circulation. Necrosis is followed by slow calcification and either late or no ossification.

W. G. Spencer,⁶ in the Erasmus Wilson Lectures, fully describes the effects on metaplasia of bone of excessive active hyperemia, which causes absorption, and of passive hyperemia which causes hyperplasia of the bone. He considers that the growth of new bone in osteitis deformans (Paget's disease) is due to venous congestion and to hypertrophy in cardiac and pulmonary conditions. He states that mechanical influences are altered in the change of blood supply and have then part in the modification of bone.

MacEwen¹³ emphasizes the mechanical influence in his work on bone, in which he shows conclusively the activity of the bone cell in the growth of new bone, relief from pressure encourages the activity of the osteogenic cell (osteoblast) and the hyperemia beyond the area of infection, causing the bone cells to become embryonic osteoblasts and to form new bone.

Todd¹⁴ says the pressure even of soft tissues easily affects the regeneration of bone.

Bier,¹⁵ in his extensive work on "Hyperämie als Heilmittel," accents active hyperemia as a part of functional activity and passive hyperemia as a relief to injuries and as a builder of new tissues. He also refers to the physical (mechanical) difference between active and passive hyperemia and to the longer contact of the venous blood in contact with tissues "where it can better unfold its activities."

Koenig¹⁶ writes, "Bone grows at the point of relief from pressure and atrophies at points of greater pressure." Elting,¹⁷ writing of osteitis deformans, says that venous dilatation may be an etiologic factor.

12 Wells, H. G. Calcification and Ossification, *Arch. Int. Med.* **7** 721, 1911.

13 MacEwen, W. Growth of Bone, Glasgow, James Maclehose & Sons, 1912.

14 Todd, T. Wingate. The Rôle of Cancellous Tissue in Healing Bone, *Ann. Surg.* **72** 453, 1920, *abst. Am. J. Orthop. Surg.* **3** 345, 1921.

15 Bier, August. *Hyperrämie als Heilmittel* ed. 6, Leipzig, F. C. W. Vogel, 1907.

16 Koenig. *Lehrbuch der Speziellen Chirurgie* Berlin, August Hirschwald, 1900, p. 778.

17 Elting, A. W. Osteitis Deformans with Report of a Case, *Bull. Johns Hopkins Hosp.* no. 128, 1901, p. 343.

Leriche and Policard¹⁸ believe that many diseases characterized by osseous new formations are dependent on absorption of bone caused primarily by circulatory disturbances. This in turn is due to a vasomotor phenomenon.

Heyman,¹⁹ writing of "Osteoporosis Relieved by Sympathectomy" reports a case which suggests that the circulation is a factor in atrophy of bone. Sympathectomy relieves spasm of the foot and osteoporosis.



Fig 1—Cardiovascular case, bone cells proliferating in metaplastic spongiosa

Maninco, Putnam,²⁰ Dercum,²¹ Spiller, Lancereaux and White²² have explained osteitis deformans and other lesions in bone as a neurotrophic disturbance acting through vascular means.

18 Leriche, R, and Policard, A. Some Fundamental Principles in the Pathology of Bone, Surg Gynec Obst **43** 308, 1926

19 Heyman, C. H. Osteoporosis Relieved by Sympathectomy. J A M A **82** 1333 (April 26) 1924

20 Putnam, James J. Hyperostosis Cranii, Am J M Sc **112** July 1896

21 Dercum, F. X., and Spiller, W. G. Bone Stryngomyelia. Am J M Sc **112** 672, 1896

22 White, E. P. C. Osteitis Deformans in Monkeys. Arch Int Med **30** 790 (Dec) 1922, Osteomalacia. Arch Int Med **30** 620 (Nov) 1922

Krogh's²² work leads one to relate the nerves vessels and endocrine glands in a composite effect on pathologic conditions of bone "Capillary tone is maintained by the sympathetics which keep them tonically contracted through the stimulus of a substance normally present in the blood" Krogh thinks the pituitary hormone in minute quantities has this effect



Fig 2—Arteriosclerotic gangrenous toe, showing new-formed cancelli, fibrous marrow, plasma cells and arteriosclerotic vessels

White²³ states that a larger calcium diet starts a neurotrophic upset, which causes perversion of the ductless glands, hyperemia and absorption of calcium

²³ Krogh, cited in The Capillaries in Health and in Disease, editorial, J A M A 80 1144 (April 21) 1923

The experiments on new formation of bone in kidneys and elsewhere indicate vascular congestion as the cause Asami and Dock²⁴ and Pearce,²⁵ obtained bone formation in the kidneys after tying the renal vessels

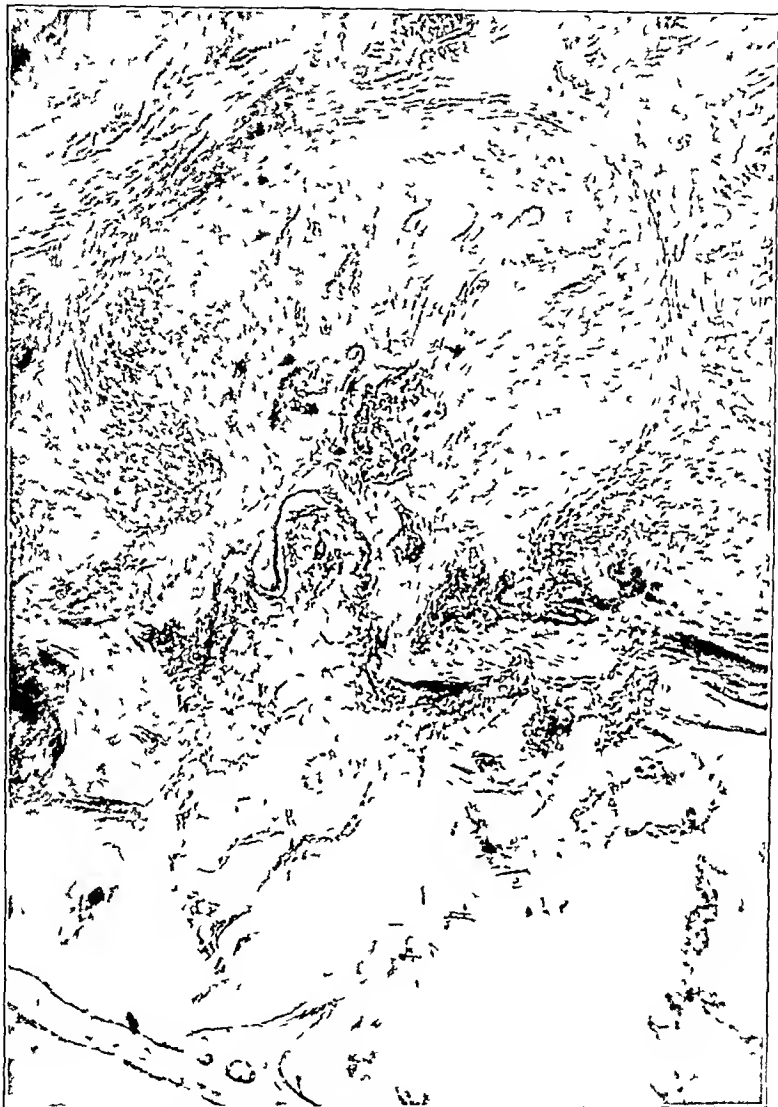


Fig 3.—New formation of bone projecting from the marrow as an osteophyte on a gangrenous toe

24 Asami, Goichi, and Dock William Experimental Studies on Heteroplastic Bone Formation, *J Exper Med* 32 745, 1920

25 Pearce, R M Later stages of the Repair of Kidney Tissue (Dog) with Special Reference to Proliferation of the Pelvic Epithelium and Heteroplastic Bone Formation, *J M Research* 20 53 (Jan) 1909

Rogers²⁶ reports osteitis without infection, quoting Preiser, who suggests injury to the blood supply as the cause of the pathologic conditions of bone. Speed,²⁷ describing the asymmetrical growth in length of long bones following osteomyelitis, mentions a case in which trauma without infection was the source of the new growth. Spencer⁶ refers to the increase in growth of bone in typhoid fever, due to the greater blood supply during the fever.

Rost's²⁸ experiments in which he produced granulation tissue and enlargement of bone by injecting noninfectious material into bone might be similarly explained.



Fig 4—Syncytium of bone cells in congested edematous cancellus of gangrenous toe

Johnson's²⁹ valuable work on the circulation in bone explains the unusual higher percentage of hyperplastic changes in the outer cortical

26 Rogers, Mark H. Traumatic Osteitis of the Wrist, *Surg Clin N Amer* **1** 697 (June) 1921

27 Speed, Kellogg. Longitudinal Overgrowth of Long Bones, *Surg Gynec Obst* **36** 787 (June) 1923

28 Rost. Experimentelle und klinische untersuchungen über chronische, granulierende Entzündungen des Knochenmarks. *Deutsche Ztschr f Chir* **125** 83, 1913

29 Johnson, R W Jr. A Physiological Study of the Blood Supply of the Diaphysis, *J Bone & Joint Surg* **9** 153 (Jan) 1927

bone in my cases. Here there is a blood supply not only from nutrient and metaphyseal vessels, but also from the periosteal circulation.

PATHOLOGIC CONDITIONS IN THIRTY CASES OF ARTERIOSCLEROTIC TOES

In six cases of arteriosclerotic toes ulceration had occurred, but in only two instances did the infiltration of leukocytes extend to the periosteum. Pus or



Fig 5—Formation of cysts by coalescence of adjacent haversian canals, arteriosclerotic toe

granulation tissue was not found in the marrow or cortex in my case. This excluded the suggestion of infection. The cartilage was softened and opaque in two cases, doubtless owing to edema. The bone was usually less hard than normal. Here edema with vital absorption must have been at work. In 10 instances it was unusually dense, the entire medullary cavity being filled by closely grown cancelli (fig 2).

Arteriosclerosis, congestion, pigmentation and edema were found in all cases. The subcutaneous tissue was fibrosed in all, spindle cells and connective tissue following the large and small vessels. Masses of sclerotic connective tissue were present in most cases. Occlusion of vessels was present in varying degrees, some being entirely obliterated by fibrous tissue, others having a narrow lumen.

The periosteum was cellular in thirteen cases and demonstrated formation of new bone in twelve. New bone was seen in the marrow in eleven cases (fig 3), deposited along old cancelli or vessels. In two cases (fig 3) this new bone



Fig 6—New bone formation on old cancelli. Fibrous marrow.

followed a cleft in the cortical bone, following vessels and forming minute osteophytic growths which caused the periosteum to bulge. The bone cells were active in sixteen cases—they were enlarged and divided and were often free at the margins of the swollen (edematous) cancelli. They were often seen in rows of pentagonal cells or as syncytium bordering the cancelli (fig 4). The haversian canals were completely or partially filled with cellular fibrous tissue in eight cases.

The lacunae were widened at the borders of cancelli in all cases. In three instances adjacent canals had coalesced, suggesting cyst formation (fig 5). Metaplasia of bone to cellular fibrous tissue was noted in five cases. The marrow was fatty in one case and fibromyxomatous or fibrous in the others (fig 6). Its

vessels were congested and frequently thrombosed, with walls thickened by young cellular fibrous tissue. Calcification of vessels was seen in three cases. New capillary loops were not uncommon (fig 7), these new capillaries were lined by active endothelial growth and had well defined fibrous walls. Small round cells or polymorphonuclear leukocytes were seen in only two cases. Plasma cells were present in large numbers in two cases, osteoblasts lined cancelli in five (fig 2), osteoclasts were present in five and minute bone spicules in four.

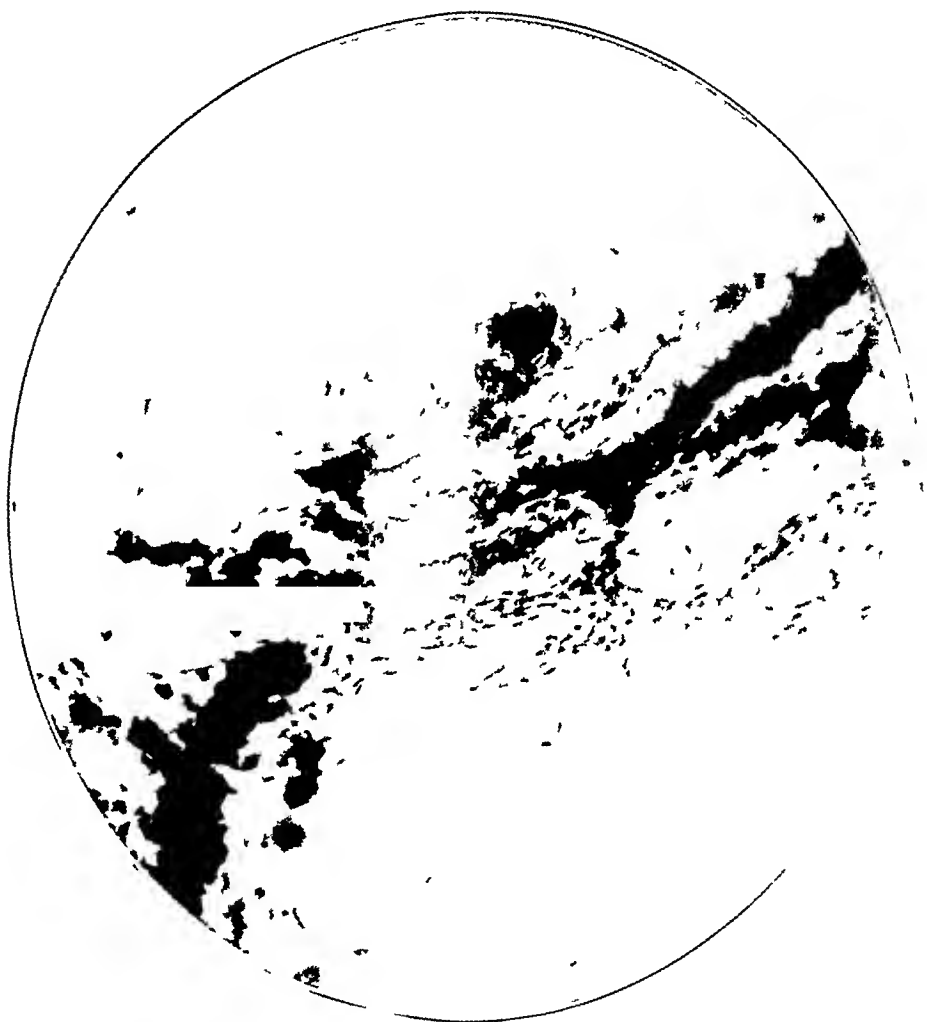


Fig 7—New capillary formation of endothelium.

DISCUSSION

Progressive arteriosclerosis is characterized by the presence of atherosclerotic plaques in the arteries. The plaques are composed of a core of lipid-rich material, the so-called "fatty streak," which is surrounded by a layer of fibrous tissue. The plaques are often associated with calcification, which is seen in the form of small, dark, irregularly shaped areas. The calcification is often associated with the presence of osteoblasts and osteoclasts, which are seen in the form of small, round cells. The calcification is often associated with the presence of plasma cells, which are seen in the form of small, round cells. The calcification is often associated with the presence of polymorphonuclear leukocytes, which are seen in the form of small, round cells. The calcification is often associated with the presence of small bone spicules, which are seen in the form of small, dark, irregularly shaped areas. The calcification is often associated with the presence of new capillary formation, which is seen in the form of small, dark, irregularly shaped areas. The calcification is often associated with the presence of active endothelial growth, which is seen in the form of small, dark, irregularly shaped areas. The calcification is often associated with the presence of well defined fibrous walls, which is seen in the form of small, dark, irregularly shaped areas. The calcification is often associated with the presence of small round cells or polymorphonuclear leukocytes, which are seen in the form of small, dark, irregularly shaped areas. The calcification is often associated with the presence of plasma cells, which are seen in the form of small, dark, irregularly shaped areas. The calcification is often associated with the presence of osteoblasts lined cancelli, which are seen in the form of small, dark, irregularly shaped areas. The calcification is often associated with the presence of osteoclasts, which are seen in the form of small, dark, irregularly shaped areas. The calcification is often associated with the presence of minute bone spicules, which are seen in the form of small, dark, irregularly shaped areas.

EFFECT OF PREGNANCY ON THE EMPTYING OF THE GALLBLADDER

A PRELIMINARY REPORT ⁴

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AND

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Boyden's ¹ observation that a meal of egg-yolk and cream caused the gallbladder of the cat to empty has formed the basis for the most important of the recent advances made in the study of the physiology of the biliary tract. Boyden's observation has been corroborated by several investigators using many species of animals. It has also been shown that the evacuation of the contents of the gallbladder is due to the contraction of its intrinsic musculature. A complete review of the recent data with regard to the emptying of the gallbladder has been presented by Whitaker ². The mechanism involved in causing the gallbladder to contract and the reason why fat should be so potent in this respect have not been determined, nor is the relation of the sphincteric mechanism of the common bile duct to the emptying of the gallbladder definitely established. Work on the latter problem was summarized recently by Giordano and Mann ³.

Reasoning from the character of similar physiologic mechanisms the origin of the stimulus causing the gallbladder to contract and to expel its contents would be considered as nervous or chemical or both. If a chemical stimulus were operative, it was thought that the part played by it could be demonstrated by feeding pregnant animals with egg-yolk and cream, and then, by removing the fetuses when the mothers' gallbladders were empty, it could be determined whether or not the fetal gallbladders had also expelled some of the contents. While there are many serious objections to this line of attack, the chief of which is the known imperviousness of the placenta to many substances, and while negative results would not be of value, if the gall-

⁴ From the Division of Experimental Surgery and Pathology, The Mayo Foundation

1 Boyden, E. A. The Effect of Natural Foods on the Distention of the Gallbladder with a Note on the Change in Pattern of the Mucosa as it Passes from Distention to Collapse, *Anat. Record* **33** 333, 1925

2 Whitaker, L. R. The Mechanism of the Gallbladder and its Relation to Cholelithiasis. *J. A. M. A.* **88** 1542 (May 14) 1927

3 Giordano, A. S. and Mann, F. C. Some Observations on the Sphincter of the Choledochus. *Tr. Sect. Path. and Physiol., A. M. A.* 1927 and *Arch. Path. and Lab. Med.* (to be published)

bladder of the fetus did empty with that of the mother it would be suggestive evidence that a chemical mechanism is responsible for the emptying.

Accordingly, a group of dogs in various stages of pregnancy was observed in the following manner. The animal was made to fast for a period of about sixteen hours and then a standard meal of egg-yolk and cream was given. Approximately from four to four and a half hours afterward, a time at which the gallbladder of the normal dog is partially or completely empty, the animal was etherized and the biliary tract explored. We were surprised to find that the gallbladder was filled, and often distended, with thick, dark bile. On the large series of dogs examined only a few showed slight evidence that the gallbladder had partially emptied. The length of time between feeding and exploration was therefore gradually lengthened. A large series of dogs in different stages of pregnancy was examined at various periods after the ingestion of the standard meal of egg-yolk and cream and in only a few, explored after a period of eight and ten hours respectively, was there any evidence that the gallbladder had even partially emptied. In contrast with these results are the results in a large series of nonpregnant dogs in which, with few exceptions, the gallbladder was found partially or completely empty approximately four hours after the standard meal had been taken.

Since the effect of pregnancy on the emptying of the gallbladder following the standard meal was so definite in the dog, other species of animals were investigated. In the only pregnant cat near term that we were able to obtain, the gallbladder emptied completely within the usual time following the ingestion of the food. A large series of pregnant guinea-pigs was examined four hours after being fed egg-yolk and cream, and in no instance was there evidence that the gallbladder had emptied. On the other hand, there is usually evidence of its emptying in the nonpregnant guinea-pig four hours after the ingestion of the fat meal.

Further experiments were carried out on the thirteen-striped gopher (*Spermophilus citellus-tridecemlineatus*), a small rodent which abounds in this region. Within a few days after coming out of hibernation in the spring, all the females become pregnant. The period of gestation is twenty-eight days⁴. It was thus possible to obtain large numbers of pregnant animals of this species. A series of these animals was obtained which included males, nonpregnant females and females at various stages of pregnancy. It was possible to study the pregnant

⁴ Drips Della. Studies on the Ovary of the Spermophile (*Spermophilus Citellus Tridecemlineatus*) with Special Reference to the Corpus Luteum. *Am. J. Anat.* **25** 117 1919.

female of the species from the time the fetuses were only a few days old through all the stages of pregnancy to term. It was found that the gallbladders of the males and nonpregnant females of the species observed four hours after the ingestion of a meal of egg-yolk and cream, were always completely empty. The gallbladder of this species emptied as completely as that of any species we observed. The degree of emptying in the pregnant female, however, depended on the stage of pregnancy. In animals observed in the early stages of pregnancy, slight emptying had occurred four hours after the taking of the "fat" meal, although in no instance, even in early pregnancy, was the degree of emptying comparable with that of the nonpregnant animal. From about the time of the middle of pregnancy to term, there was no evidence of the emptying of the gallbladder (figs 1 and 2).



Fig 1—Livers of pregnant female (left) and male gophers, four hours after feeding egg-yolk and cream. In the female the gallbladder is completely distended, while in the male it is empty.

The effect of the pregnant condition in preventing the gallbladder from emptying is demonstrated definitely in the following experiments. Pregnant dogs were given the fat meal and explored at various periods afterward. The gallbladder was distended with dark bile. The fetuses were removed, and two or three days later the animals were again fed and explored. At this time the gallbladder had emptied in the same manner and to the same extent as in the normal dog. The gallbladders of gophers which had given birth to young two days previously emptied completely after their fat food. The gallbladders emptied partially in two dogs in which the fetuses were found dead on exploratory operation.

Comparison of the gallbladders of a pregnant and nonpregnant animal four hours after a meal of egg-yolk and cream demonstrates in a striking manner the difference in the response of the biliary mechanism.

to the food. The gallbladder of the nonpregnant animal is partially or completely empty. It is flaccid, and the surface is pale. In the dog, a species in which the capsule of Glisson is reflected over and firmly attached to the gallbladder, the reflected edge of the capsule which is hidden when the gallbladder is full, can be readily seen. If the remaining content is withdrawn, it is often much lighter in color than normal because of the entrance of bile directly from the liver in the process of refilling the gallbladder. The gallbladder of the pregnant animal, on the other hand, is different. It is full and often distended four hours after the fat meal has been taken. It is dark and the bile is dark and so thick that it is withdrawn by a syringe



Fig 2—Liver and fetuses of female gopher, four hours after feeding egg-yolk and cream. The gallbladder showed no evidence of having emptied.

with difficulty. The bilirubin content of such bile, as measured in van den Bergh units, is usually a high normal (fig 3). Forty per cent iodized oil injected into the gallbladder of a pregnant dog may not be subsequently expelled following a fat meal but remains for weeks, slowly diminishing in amount.

A comparison of two gallbladders, one of a nonpregnant animal which emptied, and the other of a pregnant animal which did not empty, raises questions with regard to the so-called tests of function of the gallbladder. The gallbladder of the nonpregnant animal appeared normal grossly and emptied and filled normally. The gallbladder of the pregnant animal appeared normal grossly but did not empty normally.

Its contents showed the characteristics of stasis. Also, shortly after removal of the contents of the uterus, the gallbladder of the pregnant animal again responds normally in every respect. It is apparent that activity of the gallbladder may be influenced by factors outside the biliary tract and that the organ should neither be judged diseased or be removed because of its response to these extraneous factors, which may be physiologic.

It is obvious that in order to determine the reason why the gallbladder of the pregnant animal usually does not empty following the ingestion of the fat meal, one must know more concerning the normal mechanism of emptying.

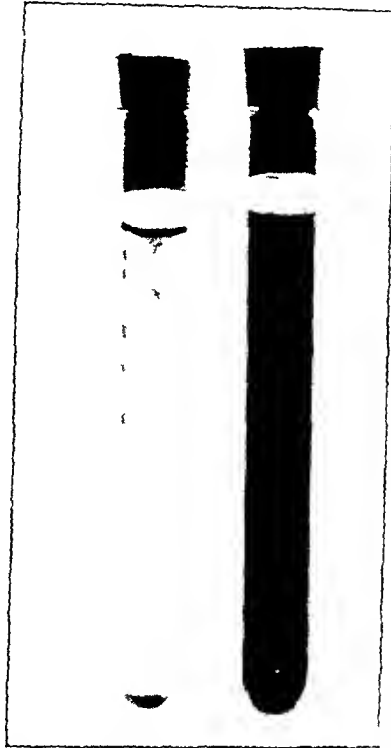


Fig. 3.—Samples of gallbladder bile taken from a nonpregnant female (left) and pregnant female four hours after feeding egg-yolk and cream. The bilirubin content of the gallbladder bile of the nonpregnant dog was 5 units (van den Bergh), while that of the pregnant female was 58 units.

In considering the cause preventing the gallbladder of the pregnant animal from emptying, the changes in the size of the abdominal cavity and in intra-abdominal pressure associated with the growth of the fetuses should be considered, not only because they are the most prominent changes occurring during pregnancy, but also because certain investigators still believe that changes in intra-abdominal pressure are important factors in causing the gallbladder to empty. There are two facts which suggest that the increase in pressure within the abdomen is a factor in preventing the gallbladder from emptying: the

relation of the degree of emptying to the stage of pregnancy particularly as noted in the gopher, and the complete emptying a short time after the fetuses have been removed. However, certain observations are not in accord with the view that the increase in intra-abdominal pressure due to the growth of the fetuses is of primary importance in the failure of the gallbladder to empty. While there was some evidence of the emptying of the gallbladder early in pregnancy, failure of the emptying process to proceed normally has been observed at a time when the fetuses were too small to affect the pressure conditions within the abdomen to any degree. The variation in the size of the abdomen associated with the ingestion of food and the expulsion of fecal material is greater in early pregnancy in the guinea-pig in which the gallbladder does not empty than in the nonpregnant guinea-pig in which the gallbladder empties completely. Furthermore, in two dogs in which the



Fig 4—Liver and fetuses of gopher four hours after feeding egg-yolk and cream, contrasted with liver of gopher which had carried paraffin balls equal in displacement to late fetuses, in the peritoneal cavity for three weeks before it was given the standard meal of egg-yolk and cream. Note differences in size of the gallbladders of the two animals.

fetuses were found dead at exploratory operation the gallbladder had partially emptied. It was also noted that the pregnant cat whose gallbladder emptied completely had a greatly distended abdomen.

Definite evidence to show that the increase in the abdominal content was not an essential factor in preventing the gallbladder of the pregnant animal from emptying was obtained by artificially increasing the contents of the abdominal cavity and then administering the standard meal. This was done as follows. Balls of paraffin (melting point 43°C) of the approximate size of the fetuses of the gopher late in pregnancy were made and sterilized in alcohol. Male and nonpregnant gophers were etherized and through a small opening in the abdominal cavity the paraffin balls were inserted in sufficient quantity to approximate the degree of abdominal distention in the pregnant animal in which

the gallbladder had failed to empty. A more accurate means of comparison was the determination of the amount of paraffin to be inserted from the amount of water displaced by the fetuses. Several days were allowed to elapse between the placing of the paraffin in the abdominal cavity and the feeding of the fat meal. When the animal had appeared normal for several days, the usual amount of egg-yolk and cream was given, and the animal was killed at the end of four hours. It was found that the gallbladder had emptied completely (fig 4).

A more important consideration bearing on the emptying of the gallbladder of the pregnant animal has to do with the mechanics of the gastro-intestinal tract. Those who have studied the emptying of the gallbladder following the fat meal are agreed that the viscus empties best when the absorption of the fat has been rapid. When the fat leaves the stomach and is absorbed from the intestine at a rate which distends the lacteals and colors the mesenteric lymph nodes white, the gallbladder is usually found to be empty, whenever the lacteals are faintly delineated, only partial emptying, if any, will take place. In the pregnant animal the fat appears to leave the stomach more slowly than normally, and the lacteals are usually only faintly delineated and not distended. The entire mechanism of the gastro-intestinal tract appears to have slowed down, and the degree of slowing is such that the emptying of the gallbladder either does not occur or is greatly delayed and incomplete.

SUMMARY

Our observations show that the gallbladder of the pregnant dog, guinea-pig and gopher usually does not empty following a feeding of egg-yolk and cream, while in the nonpregnant animal it usually partially or completely empties. Partial emptying has been noted in early stages of pregnancy, and in a few dogs it has been noted late in pregnancy. However, in no instance⁵ in the large number of animals observed did the gallbladder of a pregnant animal of these three species empty in the time and to the degree that it emptied in the nonpregnant animal. The gallbladder of one pregnant cat emptied in the same manner as that of a nonpregnant cat. A large number of pregnant cats and pregnant animals of other species must be examined before it can be accepted as a general physiologic fact that the gallbladder of the pregnant animal does not empty in a similar manner following the ingestion of the standard fat meal as it does in the nonpregnant animal. However, sufficient data have been secured in regard to three species to make it appear probable that similar observations will be made with other species including man.

The results of these experiments cannot be applied to the human being without qualification until it has been determined that the gallbladder of the pregnant woman does not empty in the normal manner.

following the feeding of fat. However, three considerations are pertinent to the subject. The pathologic conditions often associated with pregnancy which may directly or indirectly have some relation to the mechanism of the biliary tract are (1) hyperemesis, (2) eclampsia and (3) gallstones. Further observations with particular reference to the normal mechanism of the biliary tract must be made before definite conclusions can be reached.

5 Since this article was written a few pregnant dogs have been observed in which the gallbladder emptied.

REDUNDANT COLON *

HARRY GAUSS, MD

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The redundant colon is one that is too long for its owner. Kantor¹ considers it a form of congenital anomaly compatible with life and health under reasonably favorable circumstances, which under unfavorable stress and strain of life may give rise to a symptom complex of annoying and distressing manifestations. Some persons with redundant colon may never develop symptoms referable to it, others may have trouble all the time, many may be symptom-free for many years and then develop a clinical syndrome.

The whole conception of the normal anatomy of the colon, and with it the concept of the redundant colon, is undergoing a rapid transition at present. This revision is a logical supplementary study to the changed notions of the normal variations of the stomach compared to the prevailing acceptance of the so-called normal type of stomach only fifteen years ago, when the current teaching was that the normal stomach was a fundus-shaped pouch lying under the arch of the left side of the diaphragm. Today the older notions of a single stereotyped kind of stomach have been displaced by the idea that there are a series of normal types varying from the fishhook to the steerhorn type, with several intermediate types. Correspondingly, the variations of the normal colon are being studied anew, although a standard type of colon has been accepted for many centuries, ultimately, a classification will be made. At present I cannot say whether the redundant colon is a variation of the normal type, or as Kantor believes, a mild form of congenital anomaly. Certainly, at times it gives rise to a symptom complex, which easily may be recognized with the aid of the roentgenogram and which demands medical attention. The symptom complex in itself does not make it a congenital anomaly. Variations in the shape of the stomach with the accompanying inherent physiologic attributes also give rise to symptom complexes at times, yet fall within the limits of the so-called normal type of stomach. The actual length of the colon is of secondary importance, the significant feature of the redundant colon is that it is too long for the person who possesses it, so that it falls into loops and kinks which create mechanical interference with the free movements of the colonic contents. The great variation

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1 Kantor, J. L. Am J Roentgenol 12 414, 1924

in the length of the colon is brought out in the observations of Bryant² on the colons of 160 adults. He found that the colon varied in length from 3 feet and 4 inches (101.6 cm) to 10 feet and 10 inches (330.2 cm), with an average of 5 feet and 2 inches (157.5 cm). Studying the ratio of the length of the colon to the small intestine and the length of the colon to the length of the body, he observed that in the adult the ratio of the length of the body to that of the small intestine is about 1:3.7, the ratio of the length of the colon to that of the small intestine is about 1:4, that the colon of the adult about equals the length of the body, and that the small intestine is about four times the length of the body.

Davis³ studied the colons of 285 persons coming to postmortem examination for the purpose of determining the relative position of the segments of the colon, the nature of the usual angulations and the extent of deviated morphology consistent with physiologic function. He found that only 32.5 per cent of the colons conformed to the stereotyped description often seen in textbooks, even when due allowance was made for the agonal and postmortem changes, he did not consider these influences of great importance in the final conclusions. In 55 per cent of his series, he observed convincing evidences of etiologic connection for constipation. He observed distinct enlargement of the colons proximal to the constricted splenic flexure in 84 per cent of the cases; in 43 per cent the pelvic colons did not show angulation, only a slight curving being evident from the midportion of the descending colon to the segment of the rectal tube, in 12 per cent the ceca were fish-tail in shape and in 20.7 per cent decidedly pouched in form. The ascending colon was found in an oblique position in 13.7 per cent, and in 0.6 per cent it was in a horizontal position, the transverse colon was found markedly ptosed in 23.4 per cent, the splenic flexure was absent in 1.2 per cent, coiled in 1.2 per cent and the form of a clothes-pin in 2.1 per cent. The descending colon was found to be coiled between the splenic flexure and the pelvic brim in 4.2 per cent, the pelvic colon was almost straight in 16.8 per cent and acutely angulated in 16 per cent, coiled in 3.1 per cent and appeared over on the right side in 2.4 per cent. He concluded that exceptions were so frequent that the colon cannot be considered to conform to any present descriptive morphology.

From the studies of Davis and other investigators, it is rapidly becoming evident that the description of the colon that has been used for many centuries must give way to a newer broader description. Descriptions of the colon observed at laparotomy are helpful, but more than a single portion of the colon is rarely seen at operation, and when

2 BRYANT, JOHN. *Am J M Sc* 167:499, 1924.

3 DAVIS, J. E. *Am J Obst* 73:474, 1926.

symptoms arising from the colon demand surgical intervention, they usually indicate an extreme type of lesion. The minor variations, the common lesions comprising the bulk of the diversified anatomic forms of the colon, do not demand or even invite surgical intervention, and



Fig. 1—Approximately normal colon in a young woman

knowledge of them must come from postmortem examinations and roentgen-ray studies conducted on an appreciable number of persons.

My purpose in this paper is to emphasize the identity and symptomatology of redundant colon and to report some cases illustrating its characteristics.

The redundant colon is one that is too long for the person who possesses it. It is characterized by its increased length which causes loops, kinks or deviations from the normal colonic pathway which interfere with the free movements of the colonic content and give rise

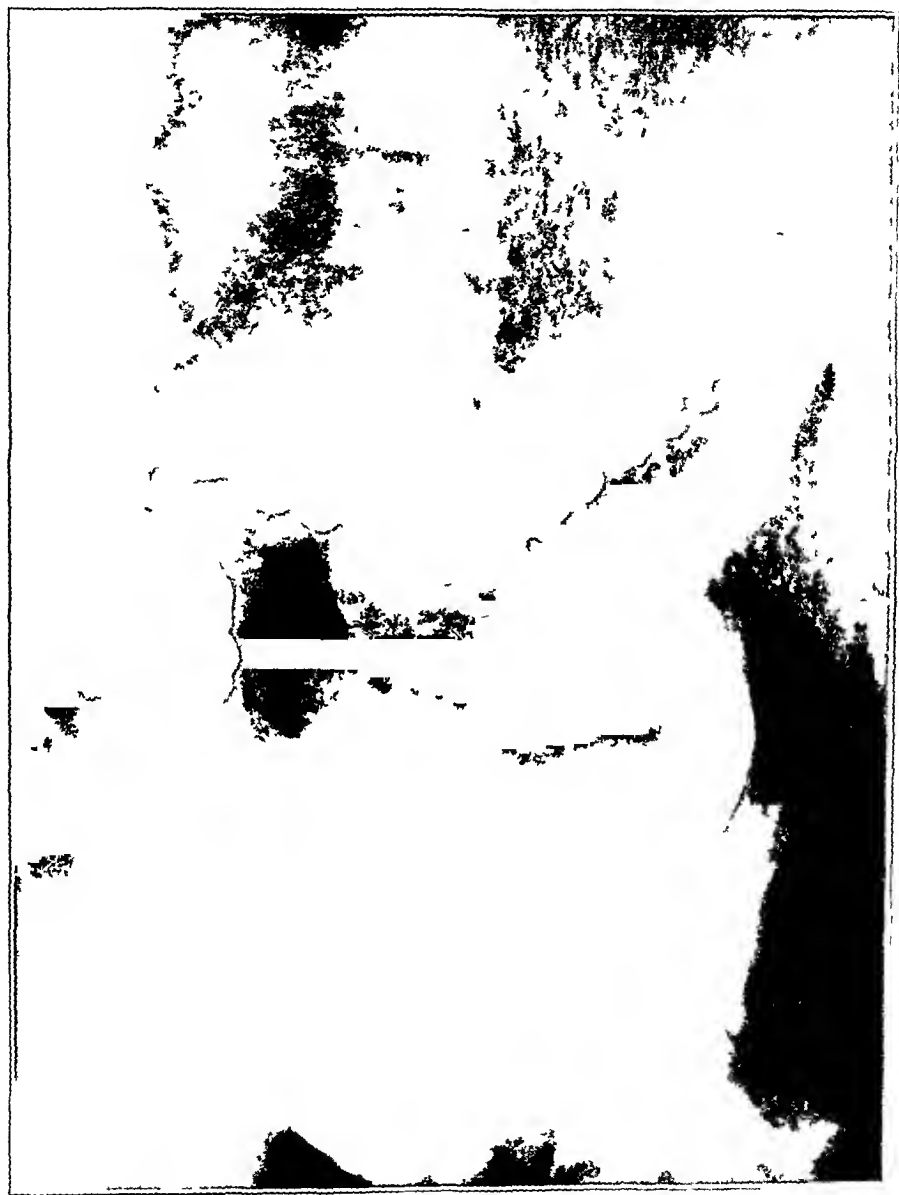


Fig. 2—Approximately normal colon in a young man

to clinical symptoms. The redundancy may be general or local. The entire colon may be too long and too loose, or a segment may be too long, thereby creating a kink, loop or double loop. According to White, three-fourths of the loops are found on the left side of the colon, either in the descending colon or splenic flexure.

PATHOGENESIS

The colon is essentially an excretory organ. Its function is the formation of feces and the elimination of them from the body. Although the colon is in continuity with the small intestine, it has few physiologic properties in common with it. The small intestine is essentially an organ of digestion and absorption. The word "small intestine" is associated with "food," the word "colon" is associated with "feces." The peristaltic wave that can be so readily observed in the small intestine is rarely observed in the colon. Only a few observers can boast of ever having seen colonic movement in human beings—Hurst⁴ mentions his own experiments and also that of Holzknecht and Case—whereas the peristalsis of the small intestine is an observation made by almost every one who has looked through a fluoroscope. The digestion of food takes place largely in the small intestine, and is considered completed when the intestinal chyme has passed through the ileocecal valve. Ferments to assist in the digestion of food are produced in the mucosa of the small intestine, there is no evidence of the formation of ferments in the large intestine. Absorption, which takes place largely in the small intestine, takes place sparingly in the colon. The subject of colonic absorption has been widely discussed and has finally resulted in a complete revision in the uses of the nutrient enema which was at one time a favorite therapeutic agent. Enemas of egg and milk, together with many other so-called nutrient enemas, have been discarded, since it has been shown that absorption in the colon is limited to water, salt, sugar and simple amino-acids. It is the last named factor, namely, the ability of the colon to absorb simple amino-acids, which is at the basis of much of the distressing symptomatology of redundant colon. Further, whereas the small intestine has an almost liquid medium to propel, the colon has a more solid, putty-like content which demands a more vigorous muscular tone. The passage of colonic contents depends largely on the contractility of the three longitudinal muscular bands. Should these longitudinal fibers become atonic, the bowel loses tone. In many patients the initial reaction is to employ cathartics and enemas or to strain at stool, but these abuses only preface a pathologic redundancy. The chemical reaction of the colonic contents is slightly alkaline. Should the alkalinity increase, the fecal mass becomes a favorable medium for the propagation of putrefactive toxicogenic organisms. Within certain limits no harm results, providing the feces are periodically expelled, but with loss of muscular tone and resulting colonic stasis, absorption of the end-products of this bacterial activity is favored. The bacteria split up the higher protein molecules into many intermediate substances, including amino-

4 Hurst, A. F. Constipation and Allied Intestinal Disorders, London Oxford University Press, 1921

acids and their derivatives, such as indol, skatol and phenol. If the decomposition proceeds further, other highly toxic substances are developed, such as putrescine, cadaverine and others, the absorption of these can produce a severe clinical reaction and may account for the toxic symptoms of chronic constipation. This view is by no means universally accepted. Among the skeptics is Hawk,⁵ who questions the specificity of the latter substances as the direct etiologic factor in disease. However, it must be borne in mind that the specific proof is a tremendously laborous chemical problem. Novello, Wolf and Sherwin⁶ apparently studied 13,000 pages of the literature dealing with the chemical side of intestinal putrefaction without solving the full problem of abnormal disintegration of amino-acid, but they succeeded in showing experimentally that as small a dose as 0.1 mg. of indol and skatol which are products of disintegration of the amino-acid typtophan, when taken into the intestine in capsules covered with salicin caused a distinct feeling of nausea followed by loss of appetite, belching and a dull headache which persisted for at least twelve hours. Even Hawk admits that the absorption of these substances is probably the chief factor in producing "bowel breath," nausea and headache in the pathogenesis of constipation. Although Novello, Wolf and Sherwin observed that phenol taken in 1 per cent solution produced no untoward effects, the corrosive action of this substance is too well known to consider the subject closed. Its local action from prolonged absorption in colonic stasis is yet to be explained.

As long as the redundant colon functions properly, it does not cause distressing symptoms, but when it becomes overfilled, twisted or packed it tends to obstruct the normal movement of the colonic contents which results in stasis and increased putrefaction, and gives rise to a whole train of symptoms, such as headache, gas distress, physical and mental fatigue, irritability, sleeplessness and other symptoms. The gases liberated in the colon also merit consideration and play a significant role in the causation of the symptoms of redundant colon. Gas distress is second only to constipation in the frequency of the symptomatology of redundant colon. Commonly it is mild but annoying; at other times it may cause acute abdominal pain as a result of increased intravisceral tension. Much of the distress from intestinal gas may be traced directly to the mechanism of the redundant colon. In the normal process of digestion certain gases such as carbon dioxide, hydrogen, nitrogen and methane and to a lesser extent hydrogen sulphide are liberated as the end products of digestion. The absorbible gases such as carbon dioxide and to a lesser extent, methane, are absorbed into the circulation and excreted through the respired air while the less absorbable gases such as

5 Hawk, P. B. and Berghelm, O. *Physiological Chemistry*, 1920, p. 107.
P. Blakiston's Son & Company, 1920.

6 Novello, N. I., Wolf, W., Sherwin, C. P. *Ann. I. N. S.* 152, 1920.

gen, hydrogen, and hydrogen sulphide, are passed through the rectum. About 1 liter of gas is passed through the rectum daily, while larger amounts are absorbed into the blood stream and so eliminated from the intestinal tract. In normal metabolism, a person suffers little from the passage of gases, but when the formation of gas is excessive or its passage is obstructed, the patient experiences abdominal consciousness then later, distress. Redundant colon may interfere with the elimination of gas in three ways: 1 By its loops, kinks, or folds, the redundant colon distorts the normal pathway for the colonic contents and may constrict the lumen of the intestine. 2 The redundant colon is a common cause of constipation, and the retained fecal masses by obstruction may decrease the lumen of the intestine. 3 By its liability to impair the circulation within the blood vessels which supply the loop by reason of pressure, torsion or traction, it may diminish the rate of absorption of the gases within the colon. The last view is supported by the experiments of Gatch, Trusler and Ayers,⁷ who have shown by experiments on animals that when the pressure of gas within an occluded loop is increased, there is a proportionate decrease in the rate of blood flow through it, which may lead to anemic stasis of the blood in that part of the intestine, gaseous distention alone may result in severe pathologic reaction, including necrosis.

Redundant colon causes constipation by altering the normal pathways of the colon or by constricting its lumen. In constipation there is an interplay of spasticity and atony with a predominance of the former. This pathologic function is also operative in redundant colon, except that in simple constipation it involves the entire colon, in redundant colon, this interplay of muscular tone may be limited to the site of the redundancy. The redundancy is not a fixed barrier to the movement of the colonic contents, it tends to become so only when it is overfilled, overdistended or kinked, when it gives rise to symptoms. When its pathway is cleared and it is functioning properly, the symptoms subside. The pathologic condition of redundant colon is that of a functional disorder superimposed on an organic condition. Neither condition is sufficient to cause its symptomatology, and the acceptance of this basis for the pathologic condition assists one in understanding the observation that this condition, which is latent since birth, may cause symptoms in the adult.

INCIDENCE

In a review of 1,000 consecutive cases of gastro-intestinal disease in private patients, White⁸ reports forty-three in which there were varying

⁷ Gatch, W. D., Trusler, H. M. and Ayers, K. D. Effects of Gaseous Distention on Obstructed Bowel, Incarceration of Intestine by Gas Traps, *Arch Surg* **14** 1215 (June) 1927.

⁸ White, F. W. *M. Clin. N. Amer.* **8** 1611 (March) 1925.

degrees of redundancy. In a similar series of 668 cases, Kantor¹ reports 92 per cent in which there were redundant colons. Bryant's² observation that there were elongated (redundant) colons in 15 per cent of his cases studied at postmortem is probably a more accurate figure, as many persons possessing the condition probably escape clinical observation. Regarding the incidence of redundant colon among the sexes, both Kantor and White report the greater frequency, about 60 per cent, in males, in spite of the many observations by surgeons of visceroprosis in the laparotomized sex. With reference to the relationship of the redundant colon to the body habitus, the reports of both Kantor and White are even more surprising. They found redundant colons in only 30 per cent of the asthenic type of persons, the remainder occurred either in the sthenic (stocky) or intermediate types.

SYMPTOMS

Some persons with redundant colon may never have symptoms; some may have symptoms occasionally, and others may have them all the time. All of the patients have an underlying predisposition to malfunction of the colon. Among the contributory causes are the stress and strain of life, wasting disease, operations, pregnancy, improperly balanced diet, insufficient exercise, bad hygiene, habit of using cathartics, worry and mental depression. Constipation is the commonest symptom. Usually it is of many years' duration and frequently the patients are habitual users of laxatives and enemas. Gas distress is the symptom of next greatest frequency. It may be manifest as flatulence, increased gas movements or increased flatus, as abdominal distention resulting from inability to move the gas, or as belching when the belching is unproductive of considerable relief, since it represents a futile attempt of the patient to rid himself of gas in the splenic flexure. Occasionally accumulation of gas in the splenic flexure may cause precordial distress and palpitation as a result of pressure under the diaphragm.

Pain in the abdomen is the next symptom of importance. This varies in degree from mild discomfort to violent colic. The pain may be general or localized. Localized pain usually corresponds to the site of the redundant colon. It is probable that it is the pain of a cecocolic colon which leads to errors in its diagnosis, and patients are frequently operated on for appendicitis. In the series of cases of Kantor and White and in my series are instances in which the patient was operated on for appendicitis and the symptoms had persisted after operation. Later the patient responded to treatment for redundancy. The pain may be associated with gas distress resulting from increased intravisceral tension. Vomiting occurs occasionally but is not characteristic. Diarrhea, another occasional symptom, probably results

mild colitis, which is caused by an irritation of the intestinal mucosa resulting from colonic stasis or by the use of vicious cathartics or enemas

DIAGNOSIS

The diagnosis is suggested by the history of colonic malfunction and confirmed by the roentgenogram showing the redundant loop. A history of constipation of long duration is suggestive, especially if it dates back to childhood, also a history of prolonged periods between stools and occasional enormous evacuations. Gas distress points to redundant colon, especially if it is persistent and occurs in young adults, and does not respond to the treatment for simple intestinal putrefaction or fermentation. The positive diagnosis can be made only by roentgen-ray examination. Both the opaque meal and the barium enema method are employed. The loop, or kink, is usually visualized best by the enema study, but its mechanism for obstruction is followed better by a study of the opaque meal. The redundant colon possesses the characteristics of a dual entity, an organic structure which under certain conditions of strain gives rise to a function disorder, and the symptoms are largely the result of its functional rather than of its organic nature. The symptoms result from the interplay of colonic spasm and atony, the constipation, the increased intravisceral pressure resulting from gas distress, and other symptoms. When these symptoms involve the greater part of the colon, they usually suggest a condition of colonic malfunction, and a study of the roentgenogram clears up the diagnosis, but when these symptoms involve only the redundant loop, they are apt to remain local and thus give rise to a confusion with disturbances of the organs in juxtaposition with the loop, the roentgen-ray examination may be omitted, and an error in diagnosis is likely to occur. Kanto¹ reports the case of a physician, aged 45, who was constipated all his life and who used cathartics habitually, his condition had been diagnosed as duodenal ulcer, later, he had had his appendix removed because of atypical recurrent abdominal pain, finally, his condition was diagnosed as redundant colon, which was confirmed by roentgen-ray examination. Patients W J D and M A N of my series are almost similar and also occur in physicians. Redundant colon must be differentiated from appendicitis—especially the so-called chronic and atypical appendicitis—from duodenal and gastric ulcer, cholecystitis, cholelithiasis and carcinoma of the colon. The fact that six of my series of eleven patients had had their appendixes removed is worthy of consideration. The differential diagnosis is made by employing every available diagnostic procedure—clinical, laboratory and roentgen ray. Of course, two conditions may coexist, but the burden of proof rests on the diagnostician.

Treatment aims at the restoration of colonic function with the minimum of intervention. A bulky diet is indicated consisting of liberal amounts of cooked fruits, including the mildly laxative fruits such as figs, prunes and apple sauce, mashed or pureed vegetables such as carrots, spinach, rhubarb and stewed tomatoes, the cereals whole wheat bread and fresh salads. Coarse substances such as bran are apt to irritate the bowel. Meat is restricted or limited to one meal a day. Lubrication is used to facilitate the movements of the colonic contents. Retention enemas of from 2 to 6 ounces (59.2 to 178.0 cc.) of any of the ordinary cooking oils, such as Mazola, are extremely useful. The patient is instructed to inject this after retiring and to remain in the recumbent position after the injection. As a rule this will be followed by an easy movement of the bowel in the morning. Oil by mouth is suggested. The liberal use of butter and olive oil in the food is recommended for the asthenic patient and mineral oil for the person who is overweight. When a spastic colon is present tincture of belladonna 10 minims (0.6 cc.), given three times a day for about a week is useful. For the high-strung or nervous patient or one who feels to relinquish his habit of using cathartics or enemas mild sedatives are given such as phenobarbital, one-half gram (0.03 Gm.), three times a day until the apprehensiveness has subsided, the belladonna, phenobarbital or other sedatives are then discontinued. Sufficient sleep and rest are essential and the "daily dozen" in the morning will be found useful to tone up the abdominal musculature as well as to stimulate intestinal peristalsis.

When the function of the colon is restored intervention is discontinued, except that the retention enema of oil and the high residue diet may become more or less a permanent part of the regimen. The great majority of patients with redundant colon who are given this treatment will return to a state of approximate well-being.

CASE REPORTS

The cases are reported as instances of redundant colon in which improvement followed medical treatment. The patients were studied thoroughly to exclude as far as possible any other pathologic condition. In every instance a careful history was taken, a thorough physical examination was made, blood count, urinalysis, test meals for the stomach, examination of the stool and Wassermann tests were made. If necessary roentgenoscopic examinations of the chest as well as of the gastrointestinal tract were made. Only the essential parts of the reports are presented.

CASE 1—W. I. D., aged 50, a physician 5 feet 11½ inches tall, height and weighing 133 pounds (60.3 kg.) had had constipation since childhood. The attacks were brought on by overeating. During the last seven years he had had regular attacks of constipation. The constipation usually occurred about the middle of the month.

Because of vague abdominal pains, atypical appendicitis had been diagnosed and appendectomy had been performed without improvement. The periods of constipation were associated with loss of appetite and nausea. The opaque enema study showed a large redundant loop in the descending colon. Treatment as outlined was instituted and was followed by improvement.

CASE 2—M. M. C., aged 52, a woman, 5 feet and 6 inches in height (167.6 cm) and weighing 145 pounds (65.8 Kg), of intermediate habitus had been con-



Fig. 3 (case W. J. D.)—Elongated loop in descending colon

stipated and had been taking enemas and cathartics for many years. She complained of loss of strength, lassitude, gas distress, bad taste, pain in the back and in the hypochondria. The appendix had been removed and ventral suspension of the colon had been performed. Roentgen-ray examination showed an elongated and looped transverse colon extending from the lower border of the costal margin down into the pelvis, also a marked colonic stasis as shown by

the presence of barium in the descending colon 120 hours after the ingestion of a meal of barium. The patient was placed on the treatment outlined and considerable improvement resulted.

CASE 3—M. K., a man aged 26 weighing 129 pounds (58.5 Kg.) and 5 feet and 5 inches (165.1 cm.) in height of intermediate habitus had been constipated ever since childhood. The appendix had been removed. The patient complained of gas distress, belching and abdominal gas distress and colic.



Fig. 4 (case M. K.)—Multiple redundancy in the hepatic flexure and in the pelvic colon.

vomiting. He used cathartics frequently. The cathartics which afforded little relief. Roentgen examination showed loops, one in the hepatic flexure and one in the pelvic colon. The transverse colon was spastic. In the third week the patient became symptomatic and in the next months while under observation.

CASE 4—T Y, a man, aged 38, 5 feet and 9 inches (175.3 cm) in height and weighing 137 pounds (62.1 Kg), underweight 25 pounds (11.3 Kg), of asthenic habitus, had been constipated for many years. He used cathartics and periodical enemas habitually. The appendix had been removed. The patient complained chiefly of gas distress, belching, flatulence and discomfort and occasional attacks of cramps in the lower part of the abdomen, associated with a rumbling sensation and constipation. Cathartics had failed to give relief. Occasionally large bulky stools were passed, followed by a sense of relief and comfort. Roentgen-ray

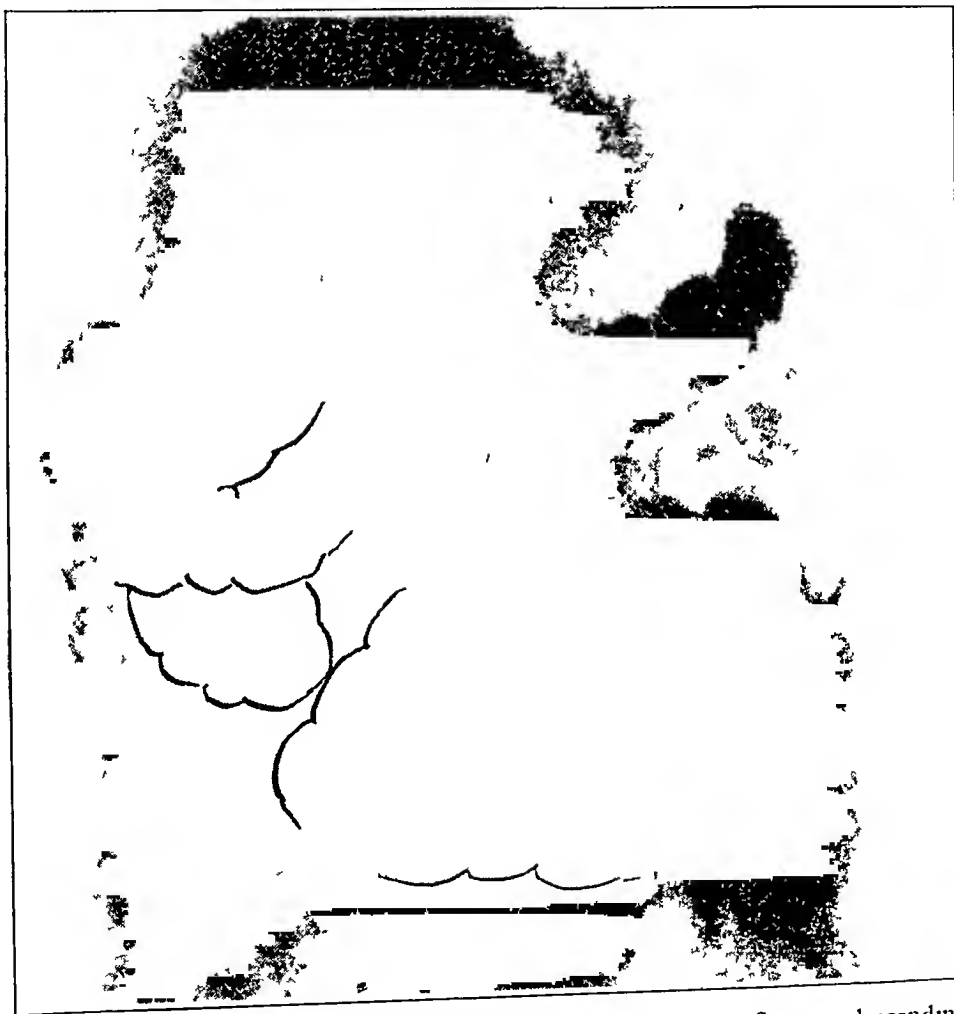


Fig 5 (case T Y) —Multiple redundancies in the hepatic flexure, descending and pelvic segments of the colon

examination showed ptosis of the entire colon, with three redundant loops, one in the hepatic flexure, one in the descending colon and one in the pelvic colon. Treatment as outlined was instituted, and considerable improvement followed.

CASE 5—G W R, a man, aged 44, a civil engineer, 6 feet and 2 inches (188 cm) in height and weighing 185 pounds (83.9 Kg) complained of a bad taste, constipation, headache and attacks of indigestion. He used cathartics habitually. The appendix had been removed. The patient also complained of gas distress, abdominal discomfort, borborygmi and lassitude. Roentgen-ray

examination showed an elongated fold with a kink in the pelvic colon. Medical treatment was instituted. Within a few weeks the patient became symptom-free, and has remained so.

CASE 6—E S, a woman, aged 48, of intermediate body habitus, 5 feet 2 inches (157.5 cm) in height and weighing 112 pounds (50.8 Kg), 22 pounds (10 Kg) underweight, complained of constipation, loss of appetite and lassitude, distress in the upper part of the abdomen, insomnia, loss of weight

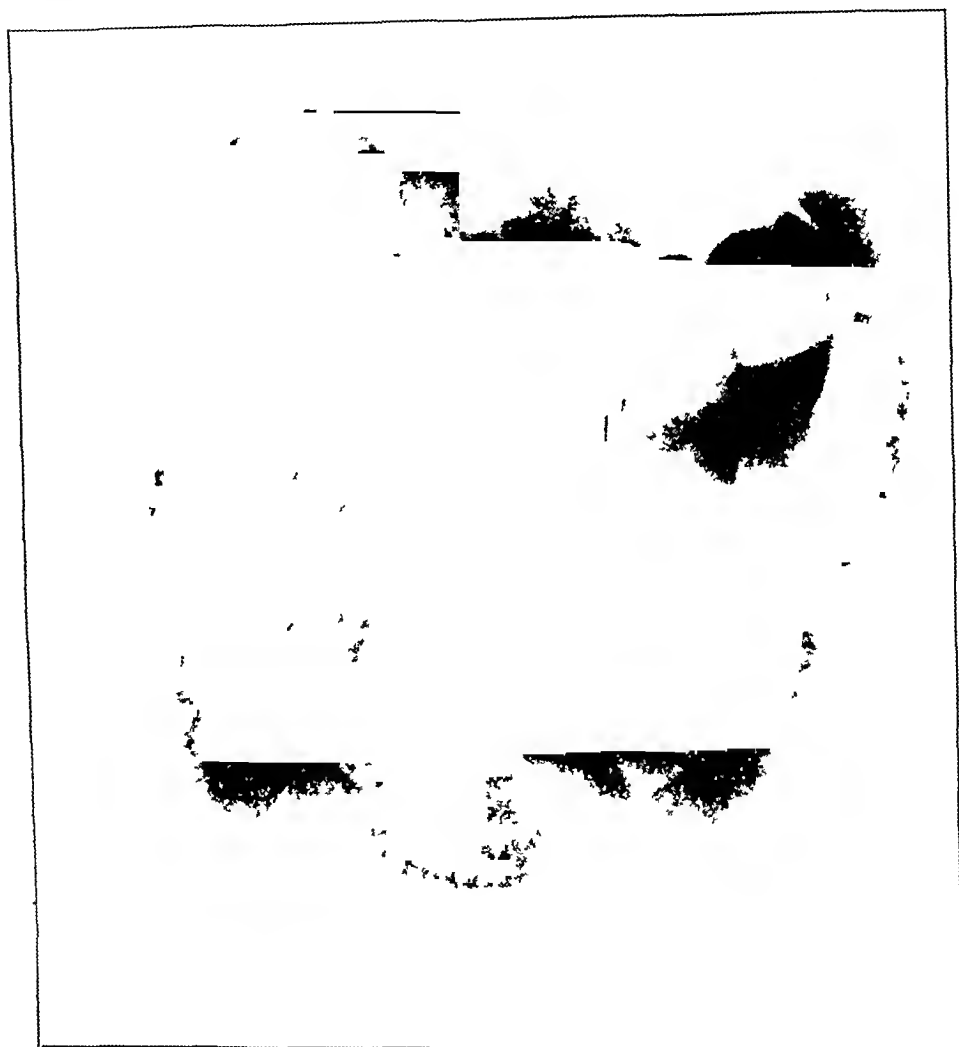


Fig. 6 (case E S)—Reduplication of the pelvic colon which ascends in spiral fashion to lie in contact with the ptosed transverse colon.

and strength. She had used cathartics and enemas for many years. Roentgen examination showed a redundant loop beginning in the lower portion of the pelvic colon and ascending by a spiral loop to the upper brim of the pelvis, where it lay in contact with the transverse colon which was ptosed. The patient was given the high residue diet and instructed to use rectal enemas of oil. Considerable improvement resulted.

CASE 7—J G, a man, aged 31, 5 feet and 8 inches (172.7 cm) in height and weighing 134 pounds (60.8 Kg) of asthenic habitus, was 20 pounds (9 Kg)

underweight. He complained of distress in the upper part of the abdomen not related to the taking of food, occasional headaches, constipation for eight years, loss of appetite and of strength. He used cathartics continually. Abdominal consciousness was present most of the time, and there were borborygmi and occasional severe attacks of abdominal pain, which were relieved by the free passage of flatus. Roentgen-ray examination showed the presence of an atonic

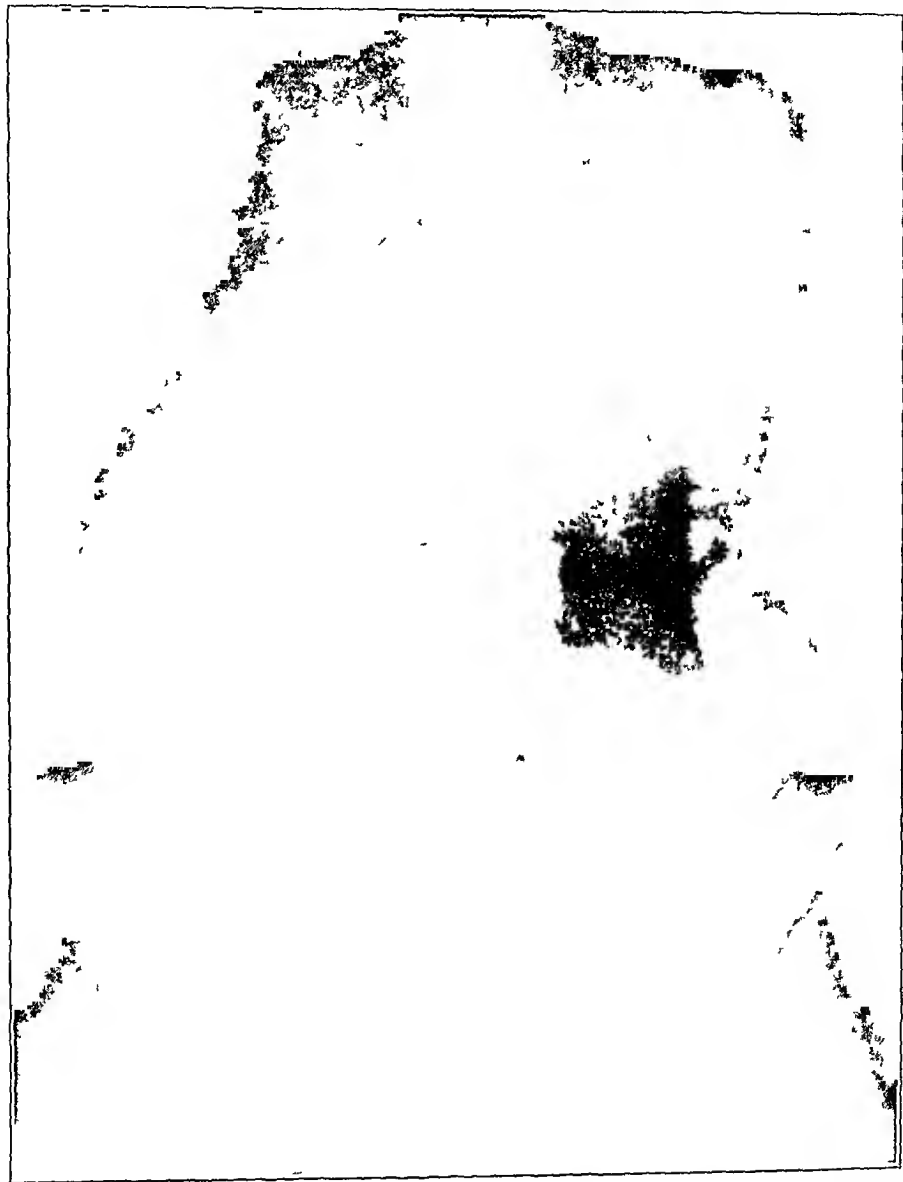


Fig 7 (case J. G.)—Redundant loop in the pelvic colon associated with dilated and atonic ascending colon.

and dilated ascending colon and a pronounced redundant pelvic loop. Rapid improvement followed the treatment outlined.

CASE 8—O. S., a man, aged 38, of asthenic habitus, 5 feet and 8 inches (172.7 cm) in height and weighing 111 pounds (50.3 Kg), was 52 pounds (23.6 Kg) underweight and inclined to minimize his symptoms or even to deny their existence. His family became alarmed over his progressive loss of weight,

and overruled his objections to physicians. He said that he had been constipated all his life, passed small, hard stools, had attacks of violent abdominal pain not localized but general in its distribution and distressing attacks of gas pains. When I first saw him, the patient was doubled up with intense abdominal pain, but he insisted that there was nothing the matter. Roentgen-ray examination showed a redundant colon, with two marked redundant loops, the most pronounced I have ever encountered, located in the transverse and pelvic colons. The transverse



Fig. 8 (case O. S.)—Extreme type of redundancies. The transverse and descending segments were filled with gas and failed to cast shadows. The transverse segment is replaced by a descending segment, the ascending oblique segment while the pelvic segment traverses the right side and descends on the right side instead of the usual left side.

colon did not exist as such; it was replaced by a descending segment, a part of which descended directly in front of the right iliac fossa, and within the pelvic brim then it ascended by a hook-like flexure to the right iliac flexure. The pelvic colon likewise was replaced by a descending segment

pelvis, then instead of descending on the left side, it traversed the pelvis and descended on the right side. The patient's response to treatment was most gratifying. Within a few days, he became symptom-free, and in six weeks (at the time of this writing) he had gained 22 pounds (10 Kg).

CASE 9—J Q, a woman, aged 51, 5 feet and 4 inches (162.6 cm) in height and weighing 125 pounds (56.7 Kg), of intermediate body habitus, complained of constipation of seven years' duration. She took an enema each night. She complained principally of gas distress, flatulence, belching and intestinal rum-



Fig 9 (case H A) —Multiple redundancies in the splenic flexure and in the pelvic colon, associated with marked ptosis

blings, occasional attacks of nausea and vomiting, headaches and vague pains in the left lower quadrant of the abdomen. Roentgen-ray examination showed the presence of a redundant loop in the pelvic colon and a spasticity of the transverse and descending colons. Treatment was followed by marked improvement.

CASE 10—H A, a woman, aged 46, 5 feet and 3 inches (160 cm) in height and weighing 125 pounds (56.7 Kg), of asthenic habitus, had been constipated all her life and had used cathartics and enemas habitually. Within a few months before she consulted me, they had lost their potency, and the patient

suffered from headaches, loginess, lassitude, gas distress and pains in the lower part of the abdomen. The appendix had been removed. The failure of the bowel to function was causing the patient considerable mental anxiety. She belched a great deal but obtained little relief from it. Roentgen-ray examination showed that almost the entire transverse colon was below the crests of the ilia while both the hepatic and the splenic flexures reached only to the level of the umbilicus. Redundant loops were present in the splenic flexure and in the pelvic colon. Considerable improvement followed medical treatment.

CASE 11—M. A. N., aged 45, a physician 5 feet and 10 inches (177.8 cm.) in height and weighing 170 pounds (77.1 Kg.), of intermediate body habitus considered himself neurotic and inclined to introspection. He had always had more or less stomach trouble. As a medical student he had been treated for

Summary of Author's Series of Cases of Redundant Colon

Case	Age	Sex*	Body Weight, Pounds	Body Height	Body Habitus	Previous Operations	Location of Redundancy	Result of Medical Treatment
1	50	♂	133	5 ft 11 in	Asthenic	Appendectomy	Descending	Improved
2	32	♀	145	5 ft 6 in	Intermediate	Appendectomy, ventral suspension of colon	Transverse	Improved
3	26	♂	129	5 ft 5 in	Intermediate	Appendectomy	Hepatic flexure, splenic flexure, pelvic	Improved
4	38	♂	137	5 ft 9 in	Asthenic	Appendectomy	Hepatic flexure, descending, pelvic	Improved
5	44	♂	185	6 ft 2 in	Intermediate	Appendectomy	Pelvic	Improved
6	48	♀	112	5 ft 2 in	Intermediate		Pelvic	Improved
7	31	♂	124	5 ft 8 in	Asthenic		Pelvic	Improved
8	58	♂	111	5 ft 8 in	Asthenic		Pelvic transverse	Improved
9	51	♀	125	5 ft 4 in	Intermediate		Pelvic	Improved
10	46	♀	125	5 ft 3 in	Asthenic		Pelvic, splenic flexure	Improved
11	45	♂	170	5 ft 10 in	Intermediate	Appendectomy, lipirotomy	Pelvic	Improved

* In this table ♂ indicates male, ♀ female.

hyperacidity, he then had had his appendix removed and another laparotomy had been performed. He had always been constipated and at one time his condition had been diagnosed as ulcer for which he had been treated. He complained of constipation, gas distress and bad taste. He used cathartics continually. The most annoying symptom was the gas distress which became so acute at times as to interrupt his social hours. He sought relief by walking and felt better following the expulsion of flatus. Roentgen-ray examination showed a marked redundant loop in the pelvic colon. This redundancy and its significance apparently had been overlooked. Improvement followed medical treatment.

DISCUSSION

Judging by the repeated attacks launched against the mechanism of the colon it is easy enough to gain the impression that nature erred in her attempt at the construction of the colon. With all the discussions raging about the stasis of the colon it might appear that nature stases

indicted for having constructed a colon so prone to faulty behavior, perhaps an overdevelopment of an anatomic form—an error of the type of the *Amphibious apatosaurus*, a colossal reptilian monster that roamed the shores of the great inland sea in what is now Colorado about 30,000,000 years ago. This colossal monster did not survive in the struggle for existence, its size was against it, and it went the way of *Archopteryx* and the saber tooth tiger. But man is an egocentric animal. He is prone to stand on the shores of the Atlantic, of the Pacific, or of the Tigris, or within the castled walls of Potsdam and look about him for more worlds to conquer. He is likely to consider himself the center of the universe, and that everything was made for his pleasure, he even vents his wrath on all things that incur his displeasure and destroys those that oppose his will. Yet, from an evolutionary point of view, man represents but a single phase of a constantly changing biologic cycle. Perfect or an experiment, man represents but an attempt of nature at a combination of biologic forces. The length of his survival is a matter of speculation.

If he has a lengthy colon, it is because he needs it. If it seems too long, it but appears lengthy because of his artificial domesticated form of existence. In the primeval forest where man lived at the time the colon was evolved, it was necessary and extremely useful. The colon represents one of nature's finest handiworks in the development and protection of her favored children. From an evolutionary point of view, the colon is partly a protective mechanism. When man descended from the trees and began to roam the plains and forest, he was pursued by his natural enemies, just as he sought their flesh as food. The excreta of an animal with its characteristic odor is one of the signs by which an animal stalks its natural prey. The species that ejects its excreta but once a day is better prepared to escape its enemies, and so survive in the struggle for existence, than the less fortunate animal that ejects its excreta more frequently, and the colon which performs this function is a proud masterpiece of protective mechanism. In the early days the colon served *Pithecanthropus erectus* of Java well. It enabled him to escape from his natural enemies, and so it was an essential factor in his successful struggle against his environment. But man no longer roams the primeval forest, instead, he sits at a desk all day and dictates letters. He eats ham sandwiches on white bread with the crusts carefully removed and ice cream, and he drinks iced tea. In the evening he goes to the "Follies" and on Sunday afternoon he plays golf, perhaps. His diet is residue-free, with all the roughage painstakingly removed. The flour he eats represents the quintessence of refinement until all the salts, as well as all the roughage, have been thrown away. He leads a sedentary existence with all muscular activity carefully eliminated by

labor-saving machines and even the use of legs that essential to all forms of progressive animal life a system of locomotion is displaced by the faster arriving automobile—and the colon appears too lengthy

SUMMARY

The redundant colon is one that is too long for its owner

It is congenital in origin

It is not materially influenced by the factors of age sex or body habitus

It is an organic structure which develops functional characteristics hence, the symptoms may develop any time during the life of the patient

The chief symptoms are constipation gas distress and abdominal pain and then attendant evils

The diagnosis is suggested by a history of malfunction of the colon and is confirmed by roentgenograms which show the redundancy

Symptomatic redundant colon must be differentiated from chronic and atypical appendicitis from gallbladder disease and from other abdominal disorders

The treatment aims at the restoration of the function of the colon with the minimum of intervention

A high residue diet and lubrication both by mouth and by rectum are the basis of the treatment Antispasmodics and sedatives are useful accessories

Surgical intervention has a place of minimum importance in the cure of the redundant colon

Under proper medical care the great majority of persons with redundant colon promptly return to an approximate state of well-being

EXTRARENAL VENOUS CIRCULATION IN A CASE OF CONGENITAL POLYCYSTIC KIDNEYS

AN UNUSUAL VARICOCELE COMMUNICATING BETWEEN THE
SPLENIC AND RENAL VEINS*

EMILE DUSKES, M D

BALTIMORE

Congenital polycystic kidneys have always been of unusual interest. Though the clinical features and pathology of this condition are amply covered in medical literature, relatively little attention has been given to the collateral venous circulation.

The pathology of the congenital polycystic kidney is well known, and the theories of its etiology are summarized by Gruber¹ in three main hypotheses: the supposition of an inflammatory origin (Virchow, Beckman, Hertz), the neoplastic conception (von Michalowicz, Chotinsky, Lejars, Koster, Nauweck and Hufschmidt) and the theory of a congenital defective development (Witte, von Mutach, Borst, Staemmler).

The recent work of Kampmeier² is noteworthy. In the study of kidneys in consecutive embryonic and fetal stages, he finds that dilations and cysts occur frequently between the convoluted tubules and the collecting ducts, and concludes that a period occurs in fetal life that is normally characterized by the presence of numerous cystic renal tubules. If the tubules fail to give way at the end of the allotted time, they may be converted into cysts. A study of general embryonic progressions and regressions makes this explanation seem plausible.

In this type of renal disease, the congenital origin of which is accepted by most investigators, it is reasonable to expect abnormalities of the renal and perirenal circulation. Oertel³ emphasizes the fact that in the normal organ the structure is continually changing.

Gross⁴ has pointed out that there is a reorganization of the arterial blood supply in pathologic conditions of the kidneys. Kuprijanoff⁵ has

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1 Gruber, G. B. *Missbildungen der Niere, Die Morphologie der Missbildungen des Menschen und der Tiere*, Jena, Gustav Fischer, 1927, pt. 3, p. 161.

2 Kampmeier, O. F. *A Hitherto Unrecognized Mode of Origin of Congenital Renal Cysts*, *Surg. Gynec. Obst.* **36**: 185, 1923.

3 Oertel, Horst. *Post-Natal Development and Pathological Organ Reconstruction in Relation to Function and Disease*, *Am. J. M. Sc.* **161**: 694, 1921.

4 Gross, L. *Studies on the Circulation of the Kidney in Relation to Architecture and Function of the Organ in Health and Disease*, *J. M. Research* **36**: 327, 1917 and **38**: 379, 1918.

5 Kuprijanoff, P. A. *Das intrarenale arterielle System gesunder und pathologischer Nieren*, *Deutsche Ztschr. f. Chir.* **188**: 206, 1924.

also noted modifications in the intrarenal arterial system in normal and in diseased kidneys

Of particular interest in this communication is the study of the readjustment or adaptation of the extrarenal or collateral venous circulation. Communications normally exist between the intrarenal and extrarenal circulation. Kolliker⁶ has described branches breaking through the renal cortex and anastomosing with the capsular vessels; he speaks of them as the "rami capsularis." Hyrtl⁷ describes these as the perforating branches, Poirier and Charpy⁸ call them the "veines emergentes of Verneuil."

The renal vein is not a closed system. Poirier and Charpy discuss three main collateral circulations: (1) "veines emergentes of Verneuil" which pass from the substance of the kidney and enter the inferior vena cava, the lumbar or the spermatic vein, and which are especially seen on the posterior surface near the hilum of the kidney; (2) "veines adipeuses," which circumscribe and receive blood from the fatty capsule and through small venules from the surface of the kidney and which communicate with the adjacent veins, such as the renal, capsular, spermatic, inferior phrenic, ureteric and lumbar, and (3) the "anastomosis réno-azygo-lumbar," which consists of a large trunk from the posterior aspect of the renal vein, communicating with the lesser azygos (hemiazygos) and the first lumbar vein.

Cruveilhier⁹ found anastomosing branches between the left renal and the superior mesenteric veins. The venous anastomoses about the kidney have been separated into five essential groups by Tuffier and Lejars,¹⁰ as follows: capsular, renal, capsular, mesenteric, capsular, supra-renal, capsular, spermatic or ovarian and capsular, lumbar (fig. 1).

Geberg¹¹ injected the kidneys of dogs and cats and confirmed the foregoing conclusions. Lick¹² observed that the most important anastomosis in man occurred among the renal, ureteric and supra-renal

6 Kolliker, A. *Handbuch der Gewebelehre des Menschen*, ed. 5, Leipzig, Wilhelm Engelmann, 1867, p. 505.

7 Hyrtl, *Das Nierenbecken der Säugetiere und des Menschen*, Denkschriften der k. Akademie, Wien, 1872. Quoted by Dehoff, I. "Die inneren Zellen des Capillarsystems in der Nierenrinde des Menschen," *Virchows Arch.*, 1920, **Ann.** 228, 134.

8 Poirier and Charpy, *Traité d'anatomie humaine*, Paris, Masson et Co., 1901, vol. II, pp. 994-1014.

9 Cruveilhier, J. *Anatomie descriptive*, Paris, Pichet, 1826, vol. I, p. 306.

10 Tuffier and Lejars, "Les veines de la capsule adipeuse rénale," *Arch. de physiol. norm. et path.*, series 5, **3**, 41, 1891.

11 Geberg, A., quoted by Dehoff, "Ueber die Zellen des Capillarsystems in der Nierenrinde des Menschen," *Internat. Monatsschr. f. Anat. u. Physiol.*, 1920, **vol. 2**.

12 Lick, F., "Die inneren Zellen des Capillarsystems in der Nierenrinde des Menschen," *Internat. Monatsschr. f. Anat. u. Physiol.*, 1920, **vol. 2**, 275.

REPORT OF CASE

History—A colored woman, aged 45, gave the anamnesis frequently associated with this type of lesion of the kidney. She had had the usual diseases of childhood, she had had typhoid fever at the age of 13 and had shown clinical symptoms of syphilis. At autopsy there was gross evidence of syphilis, and the Wassermann reaction was positive. She had had ten pregnancies, four of which resulted in miscarriages. The other six resulted in living children, of which one survived. Death resulted from renal insufficiency. The polycystic condition of the kidneys was entirely unsuspected.

Autopsy—Typical bilateral congenital polycystic kidneys were found at autopsy. The right kidney was matted down by surrounding adhesions to the gallbladder, liver and ascending colon, which complicated study of its vas-

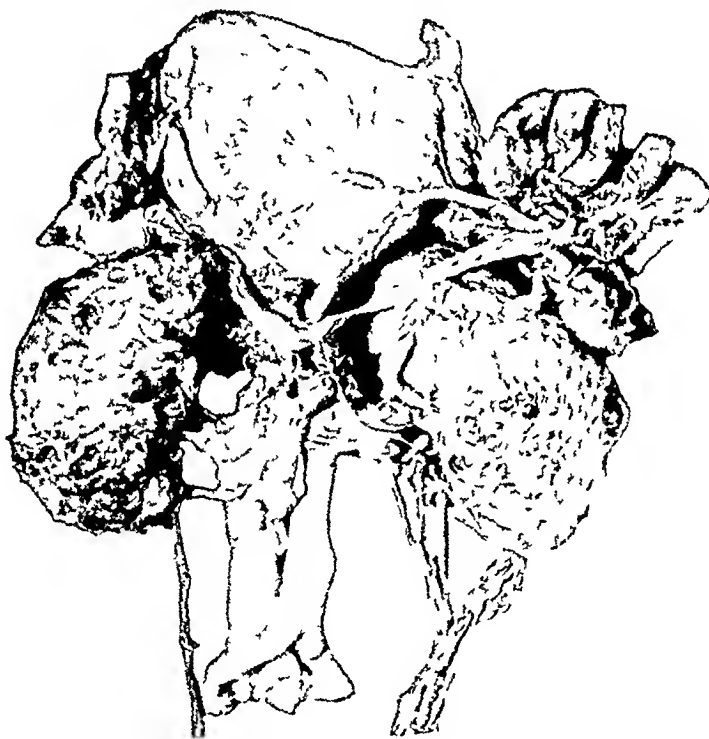


Fig 2—The anomalous vessel is seen crossing the upper third of the left kidney. The folds of the lienorenal ligament have been removed, exposing the varicocele between the renal and splenic veins.

cular system. The veins and venules on the left side were somewhat more prominent than usual, but particularly interesting was a marked enlargement of a capsular branch traversing the anterior aspect of the kidney, joining the splenic and renal veins and emptying into the latter by a triple base. In the lienorenal ligament, a marked tortuosity was found, a definite varicocele (fig 2).

The right kidney was surrounded by a thickened peritoneum adherent to the gallbladder, liver and hepatic flexure, and the perirenal fat was markedly indurated. The vessels of the right kidney were prominent and numerous, but no vascular changes or anomalies were evident (fig 3). The surface veins of the left kidney were prominent, and the fatty capsule contained numerous dilated veins. The lienorenal ligament was enlarged, and a definite varicosity

connected it with the splenic and renal veins. Minute twigs connected the inferior surface of the diaphragm with the spleen and the colon. Engorged venules extended from the kidney to the parietes and to the posterior abdominal wall. Both kidneys, the spleen, part of the pancreas and part of the diaphragm, together with the large vessels, were removed en masse.

The kidneys presented the typical appearance of congenital polycystic disease. The right kidney measured 116 by 62 cm and was from 5.2 to 6.4 cm thick. The general conformity was oval. The surface was unevenly covered with innumerable large and small cystic elevations which varied in diameter from 1 mm to 18 cm and in color from a clear serous to light straw brown, intense brown mahogany or even to Indian red or blue. Resistant, firmer, more solid areas were irregularly scattered over the surface. The renal capsule was thin and was separated with difficulty from the underlying surface.

On section the cysts had a smooth, glistening lining. They were present everywhere, with only scattered areas of renal parenchyma remaining, especially near the extremities. The contents of the cysts varied from a thin, watery

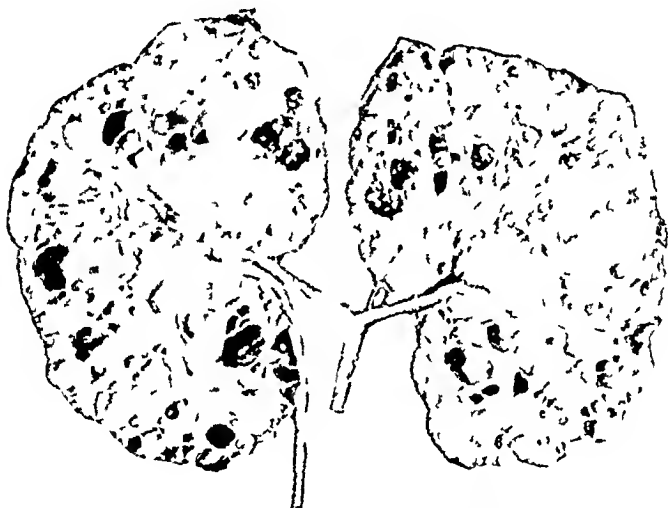


Fig. 3—Section of the right kidney, showing the typical congenital polycystic kidney. Note the cysts of various dimensions, the absence of a renal cortex, the small remains of renal parenchyma and the distorted calices.

substance to a colloid. There was no differentiation into cortex and medulla. The cysts involved the whole structure. The pelvis and calices were definitely flattened and compressed somewhat irregularly. The ureter was normal.

Many enlarged venules and a few minute perforating twigs overlay the fibrous capsule. The renal vein and artery were normal.

The left kidney was similar, and measured 118 cm in length, from 5.4 to 6.3 cm in width and from 4.1 to 7.2 cm in thickness. An examination of this organ (with its blood vessels) showed a distinct venous anomaly. Arising from the renal vein through three branches at a point 16 cm from the renal pelvis, there was a large flattened vein, which measured 12 cm in diameter. This vein received the suprarenal vein (fig. 4), and as it traversed the upper third of the kidney in a somewhat elongated horizontal S manner, it also received branches from the fibrous and fatty capsules. About the center of this renal course, a large branch measuring 3 mm in diameter coming from the

surface of the kidney emptied into the inferior border. The vein passed into the lienorenal ligament and was held in its folds. Here the vein was tortuous and wormlike. It received a small branch from the lower pole of the spleen, minute twigs from the pancreas and diaphragm and numerous venules from the perirenal adipose tissue. It communicated with the splenic vein at a point 12 cm from the hilum of the spleen.

For a distance of 4 cm from the junction with the splenic vein, the anomalous vessel continued as a single trunk measuring 0.8 cm in diameter.

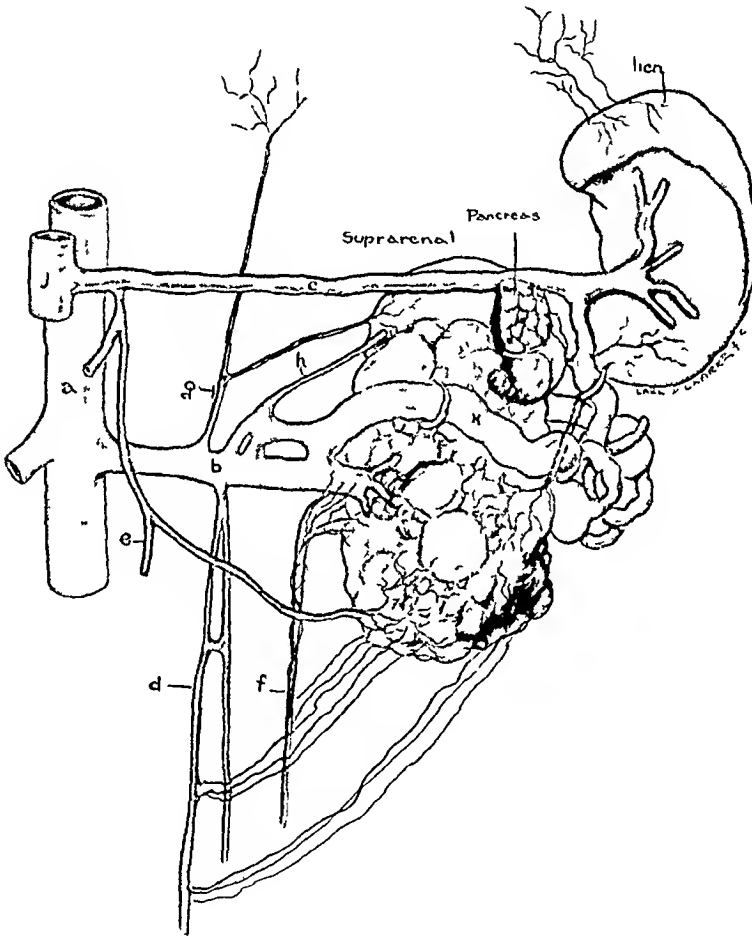


Fig 4—Semischematic drawing illustrating the more important vessels and the collateral anastomoses, *a* is the vena cava inferior, *b*, the vena renalis, *c*, the vena lienalis, *d* the plexus venosus ovaricus (spermaticus), *e*, the vena mesenterica inferior, *f*, the plexus venosus uretericus, *g*, the vena phrenica inferior (anastomose reno-azygo-lumbar)), *h*, the vena suprarenalis, *j*, the vena portae, and *k*, the anomalous vein.

Here it bifurcated into two channels, both measuring 15.3 by 0.5 cm (fig 5). At the margin of the kidney, these channels united into a single vessel 9.2 cm in length. The total length of the varicocele from the renal to the splenic vein was 38.5 cm. Throughout its course the vessel was tortuous and irregular, with large knoblike dilatations frequently interposed.

From the capsule of the kidney many fine vascular branches crossed the surface, but they were chiefly at the sides and margins, extending in devious directions. A few small branches entered the suprarenals at the upper pole. A few small venules arose from the surface of the hilum and emptied into the anomalous vein. In addition, capsular branches reached and accompanied the ureter. The lower pole of the kidney sent branches along the course of the ureter and to the ovarian vein. A branch went to the inferior mesenteric vein to join the splenic before emptying into the portal vein. Capsular vessels in the lateral border were traced to the diaphragm.

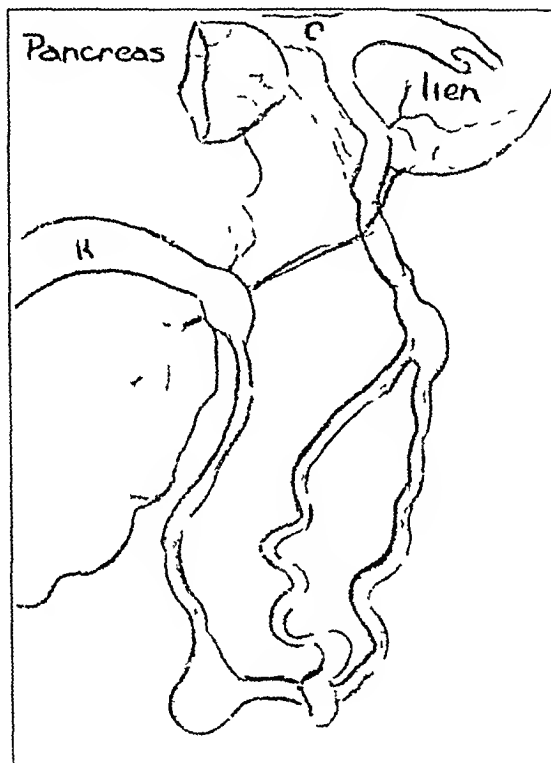


Fig 5—The varicocele spread out to show its form and comparative size

SUMMARY

A case of congenital polycystic kidneys is reported. No general abnormality was present, but in a study of its collateral venous circulation, a hitherto unrecorded condition was found, a varicocele communicating between the splenic and renal veins. I believe that this condition arises as an early embryonic adjustment for a deranged venous supply. It begins as a normal minute communicating twig between the capsular and splenic venules and becomes abnormally large. Through

this reasoning the condition is explained, not only as a persistence of a normal condition, but also as an ontogenetic or antenatal accommodation to changes in morphologic structures. Anomalies have been observed repeatedly in congenital polycystic kidneys. In this case neither skeletal nor visceral tissues showed demonstrable deviations, with the single exception of this vascular monstrosity.

THE BILATERALITY OF THE LIVER

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Since the statement of Duvernoy¹ in 1835, that the number of lobes in the liver described by different authors was truly remarkable, there have been many further plans proposed for dividing this organ into separate anatomic areas. At the present time the majority of modern textbooks describe the liver as consisting either of two lobes separated by the falciform ligament, or of some variation of the familiar "five lobes, five surfaces and five fissures". A review of the literature will easily convince one that the question has been considered from different standpoints with just as diverse results, so that a correlation of the various embryologic, anatomic and morphologic conceptions is rather difficult. We shall review in some detail the literature on the subject and present evidence of an anatomic and pathologic nature which may aid in its solution.

HISTORICAL REVIEW

Duvernoy¹ (1835) from a comparative anatomic study, concluded that the mammalian liver was composed of a principal lobe divided into two or three subsidiary parts and lying between a right and a left lobe. This plan was somewhat modified in the liver of man, so that only a principal lobe remained with a prominence equivalent to the right lobule on its lateral surface. He held that the chief factors in the variation of the lobes and fissures were the character of the food and the correlated configuration of the stomach. Rolleston² (1861) proposed to speak of the liver as divided into three parts, the right, left and suspensory lobes, using the suspensory or falciform ligament as a center of division. This landmark has been almost universally used by subsequent investigators.

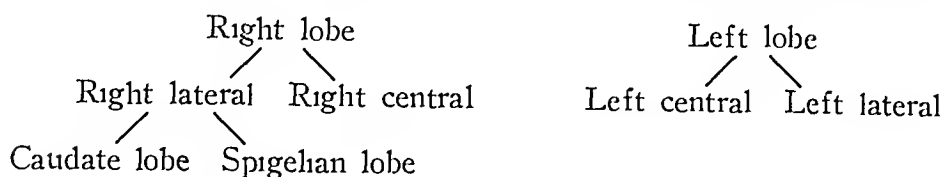
Flower³ (1872), after studying livers from almost every variety of mammal, made perhaps the first really important contribution to the subject. Following Rolleston, he considered the liver to be pri-

1 Duvernoy, quoted by Bradley. *J Anat & Physiol* **73** 259, 1909

2 Rolleston, G. On the Homologies of the Lobes of the Liver in Mammalia, *Brit Assn Rep Notices and Abstracts*, 1861, p 174

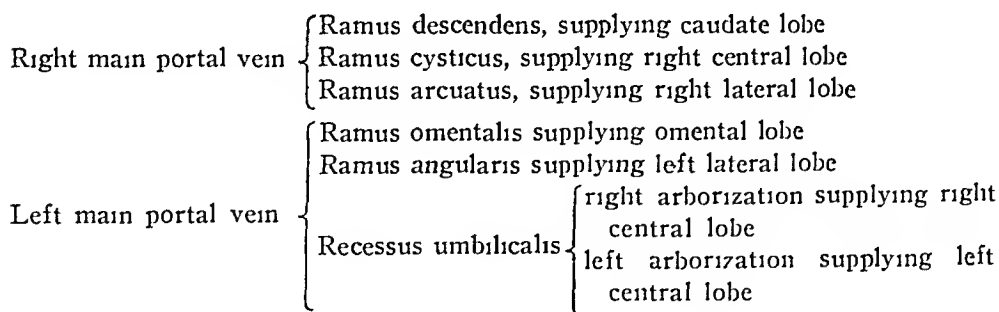
3 Flower, W H. Lectures on the Comparative Anatomy of the Organs of Digestion of the Mammalia. *M Times & Gaz* **1** 291, 392, 451, 507, 561, 621, 678, **2** 19, 59, 115, 319, 371, 427, 591, 645, 1872

marily divided by the remains of the umbilical vein and ductus venosus into the right and left halves. Each half was then subdivided thus



Four principal lobes were thus recognized with the caudate and spigelian lobes attached as appendages to the right lateral subdivision. Flower found that the liver in all mammals, except the gorilla, resembles that of man to a fairly great extent. The differences in the gorilla caused him to note either that the modifications of the liver are not characteristic in related animals, or that the gorilla ought not to occupy the position in the evolutionary system hitherto accorded to it.

Rex ⁴ (1888) considered the arrangement of the blood vessels within the liver in relation to the form of the organ as a whole. Independently, he confirmed the work of Flower, although his use of a different terminology makes a clear understanding of his meaning somewhat difficult. He found that the right and left branches of the portal vein had a remarkably regular distribution by means of secondary branches within the liver, not only in man, but in related animals. Therefore, he felt he could trace the process of development not only through the lobes, but also through the branches of the portal vein. The following scheme shows the relation of vessels to lobes according to Rex:



This arrangement is practically the same as that of Flower, except that the term omental is used for spigelian. Here again the falciform ligament was used to divide the liver primarily into halves. Rex did not attribute the presence or absence of fissures to the vessels, but stated that homologous regions of the liver in different animals may have homologous vessels whether fissures are present or not. Ruge ⁵

⁴ Rex, H. Beiträge zur Morphologie der Saugerleber, *Morphol Jahrb* **14** 517, 1888

⁵ Ruge, G. Der Verkürzungsprocess am Rumpfe von Halbaffen, eine vergleichend anatomische Untersuchung, *Morphol Jahrb* **18** 185, 1891

(1892), however, attributed the variations in the conformation of the liver to the embryologic modification in the form of the trunk and to a flattening of the dome of the diaphragm, rather than to any intrinsic influences. In the same way, Keith⁶ (1899), writing of the disappearance of the fissures in man and anthropoid apes, held that as a result of the assumption of the upright posture, the dorsal mesentery has acquired a more complicated mode of fixation, consequent on the removal of the support formerly afforded the liver by the ventral abdominal wall. The more extensive fixation of the liver to the dorsal abdominal wall is thus correlated with the disappearance of the fissures. It has been pointed out several times that Keith's explanation does not show why an undivided liver is found outside of primates, in mammals with a prone position and an uncomplicated dorsal mesentery. Again, from a study of the livers of anthropoids and those of human fetuses from 2 months to full term, Thomson⁷ (1899) found little on which to base definite conclusions. Like Flower, he considered that the gorilla showed the greatest subdivision, possessing separate caudate and subdivided right and left lobes. In the orang-utang and gibbon the caudate lobe also was usually separate. In the human fetus the liver was remarkable for the proportionate size and prominence of the spigelian and caudate lobes, the latter in many instances being separated from the right lobe by a deep fissure along its anterior border. He held that the appearance of anomalous fissures and clefts on the under surface of the right lobe of the liver of man could thus be accounted for by reference to the fetal condition and to the arrangements of the lobes in the anthropoids. It is noteworthy that Thomson attributed more importance to the caudate and spigelian lobes than any previous or subsequent writer.

From the embryologic aspect there is much of interest, but little that is not extraordinarily contradictory. Brachet's⁸ contribution (1895) is of interest in that he recognized the fact that the lobes are developed in conjunction with the vessels. Thus, he found that the liver of the rabbit consisted essentially of three lobes: (1) a median lobe occupying the ventral portion of the organ and consisting of that part developed in conjunction with the two umbilical veins, (2) a left lateral lobe proceeding from the primitive left omphalomesenteric lobe which develops along the vein of the same name, and (3) a right lateral

6 Keith, A. The Position and Manner of Fixation of the Liver of Primates and the Part These Factors Play in the Lobulation of the Liver, *J. Anat. & Physiol.* **33** 21, 1899.

7 Thomson, A. The Morphological Significance of Certain Fissures in the Human Liver, *J. Anat. & Physiol.* **33** 546, 1899.

8 Brachet, G. Recherches sur le developpement du diaphragme et du foie chez le lapin, *J. de l'anat. et de la physiol.* **31** 511, 1895.

lobe bearing the same relationship to the right omphalomesenteric vein, with the so-called spigelian and caudate lobes as mere appendages

In his more recent embryologic monograph, Mall⁹ (1906) deals extensively with this question of lobular constitution. Admitting that the liver is primarily a bilobular organ he says

In the embryo of the end of the fifth week the right and left portal twigs have begun to divide, and from the recessus umbilicalis a new group of veins have formed and radiate into the middle and left lobes of the liver. On the hepatic side the left branch has divided into two trunks and two new branches have appeared the vena cava inferior and the vena hepatica media which has its terminal right and left branches. The right omphalo-mesenteric vein is still present and the ductus venosus is well marked. In this case the liver is formed of four main lobules and with the subdivision of the middle and left hepatic veins into two branches each, six primary lobules are seen to correspond with the six primary lobes of the mammalian liver. With the completion of six lobules we recognize fully the adult form of the liver. Each lobule now represents one of the six lobes of the mammalian liver, each of the primary lobules is to expand into a whole lobe.

Bradley¹⁰ (1909) took strong exception to this last statement. He considered these so-called lobes merely arbitrary divisions of the organ made for the purposes of description, and as such they could have little anatomic value. The umbilical fissure in man and mammals was not a true fissure, in that it might be late in appearing and might even be absent in the adult. He pointed out that its occurrence depends on the presence of the left umbilical vein, and that if the right umbilical vein were to persist, two fissures would occur, thus making manifest the error of considering one of them as a dividing line in the anatomic structure of the liver. From an examination of the portal and hepatic veins in a large number of embryos of pigs, he came to the conclusion that the mammalian liver consisted essentially of three lobes—a central and two lateral. The central lobe was not divided by the falciform ligament, as Flower concluded, although otherwise their conceptions were practically identical. Comparing the nomenclature of these two writers, the following resemblances are noted

Bradley	Flower
Central lobe	Right central lobe
Right lateral lobe	Left central lobe
	Right lateral lobe
	Caudate lobe
	Spigelian lobe
Left lateral lobe	Left lateral lobe

⁹ Mall, F. P. A Study of the Structural Unit of the Liver, *Am J Anat* 5 227, 1906

¹⁰ Bradley, O. C. A Contribution to the Morphology and Development of the Mammalian Liver, *J Anat & Physiol* 43 1, 1909

With these divisions, Bradley follows Brachet in identifying various embryonic veins, the umbilical veins arising in conjunction with the central lobe, the right and left omphalomesenteric veins with the lateral lobes

So much for the evidence from the embryologic and comparative anatomic standpoints Duvernoy recognized two lobes, Rolleston, Brachet and Bradley, three, Flower four and Rex and Mall, six The majority of these authors allow of further subdivisions of the principal lobes although there is little uniformity in the areas of hepatic tissue contained within their boundaries

The physiologic and purely anatomic aspects, however, are interesting Glenard¹¹ (1890), from a series of careful clinical observations, came to the conclusion that definite alterations in size, tenderness and consistency, occurred in the lower palpable border of the liver in a variety of diseases Thus, in diabetes, the right lobe was found to be the seat of most marked change, in gastritis from alcoholism, the left lobe was most affected, and in biliary disease the central portion From this he supposed that parts of the liver were of independent vascular supply and drained definite areas of the gastrointestinal tract Wertheimer and Lepage¹² (1896), in the course of other experiments, found that on injecting sulphindigodate of soda into the right or left hepatic duct, no transference took place from side to side, therefore, they concluded that the right and left lobes were distinct in their biliary drainage It remained for Cantlie¹³ (1898) to state the matter clearly After observing the liver of a Chinaman at necropsy, in which there was complete atrophy of the right lobe, due to abscess, and compensatory hypertrophy of the left lobe, he injected the portal vessels of several livers and found that the gallbladder occupied a central position in the organ with the true right and left lobes on each side of it The line of separation ran from the fossa for the gallbladder to the entrance of the hepatic veins into the inferior vena cava Injections into the arteries and bile duct were not so satisfactory, but on the whole were confirmatory of his hypothesis

11 Glenard, F Des resultats objectifs de l'exploration du foie chez les diabetiques, *Lyon med* **44** 5, 80, 115, 189, 259, 1890

12 Wertheimer, E, and Lepage, L Sur les voies de resorption de la bile dans le foie, *Compt rend Soc de biol* **48** 950, 1896

13 Cantlie, J On a New Arrangement of the Right and Left Lobes of the Liver, *Proc Anat Soc Gr Britam & Ireland* **32** 4 (June) 1898

Seregé¹⁴ (1901), apparently unaware of Cantlie's communication, confirmed and extended the observations of Glenard. By the injection of methylene blue into each lobe, he showed that there was a distinct independence of blood supply in the two sides, the line of separation corresponding to that described by Cantlie. Moreover, after the injection of small amounts of India ink into the splenic and mesenteric veins and its discovery in definite situations within the liver, he stated that within the portal vein two blood currents existed, with different characteristics. These currents arose from the mesenteric area on the one hand and the splenic on the other, the former going to the right lobe and the latter to the left. He supported his theory with numerous clinical observations. This work was repeated by Glénard¹⁵ (1901), with identical results. Seregé¹⁶ (1902), by determining the urea content of the right and left lobes of the liver in the dog following a meal of chopped meat given after a period of fasting, found marked differences in the urea content during the various phases of digestion. During the first two hours the left lobe contained more than the right, from the second to the fourth hour, the right contained more than the left, and at the eighth hour, the amount was the same on both sides. Silvestri¹⁷ (1905), from the same type of experiment, confirmed the functional autonomy of the two sides of the liver to a certain extent, but considered the difference slight. Loeb¹⁸ (1907), following the subcutaneous injection of 0.9 Gm of potassium iodide, found that the right lobe contained much more than the left one hour after injection. This was partly confirmed by Wells and Hedenburg¹⁹ (1912). Looten²⁰ (1908), using indigotate of soda and carmine as injection material in twenty-five livers obtained from cadavers, could not demonstrate an intrahepatic capillary circulation between the bile

14 Seregé. Contribution à l'étude de la circulation du sang porte dans le foie et des localisations lobaires hépatiques, *J de med de Bordeaux* **31** 271, 291, 312, 1901

15 Glenard, F. Note sur les localisations lobaires hépatiques, *Bull et mem Soc med de hôp de Paris* **3**, 18 386, 1901

16 Seregé. Sur le teneur en urée de chaque lobe du foie en rapport avec les phases de la digestion, *Compt rend Soc de biol* **54** 200, 1902

17 Silvestri, T. Sull' indipendenza funzionale ed anatomica dei lobi del fegato, *Gazz d osp* **26** 570, 1905

18 Loeb, O. Die Jodverteilung nach Einfuhr verschiedener Jodverbindungen, *Arch f exper Path u Pharmacol* **56** 320, 1907

19 Wells, H. G., and Hedenburg, O. F. Studies on the Biochemistry and Chemotherapy of Tuberculosis. I. The Permeability of Tubercles for Iodine Compounds and Proteins, *J Infect Dis* **11** 349, 1912

20 Looten, J. Contribution à l'étude de l'indépendance vasculaire du foie droit et du foie gauche. Existe-t-il ou non un double courant sanguin dans la veine porte? *J de l'anat et de la physiol* **44** 87, 1908

ducts of the two sides. Like Wertheimer and Lepage, he felt obliged to consider the liver of man, not as a unique and compact mass, but as formed of two lobes clearly separate and independent. Gilbert and Villaret²¹ (1909), while confirming the existence of a gross independence of the two lobes, denied the absence of a capillary anastomosis in the median plane. The whole question was reviewed by Bauer²² (1909), who, from injection experiments with India ink, concluded that it was impossible to distinguish a mesenteric and a splenic area in the liver. The so-called line of demarcation between the right and left lobes was by no means constant, representing merely a zone of union between two portohepatic venous systems such as occurs in many other places in the liver. The separation was not absolute, and injection fluids readily flowed from one side to the other. Bartlett, Corper and Long²³ (1909), however, from the absorption of emulsified fat and copper in isolated intestinal segments, considered the functional independence of the two lobes to be partially established, with some slight overlapping of the two sides. They found a dual portal current in the dog, the blood from the stomach, spleen, duodenum, first portion of the jejunum and rectum flows mainly to the left lobe, while the blood from the lower jejunum, ileum and first portion of the large intestine flows mainly to the right lobe.

PURPOSE AND SCOPE OF STUDY

In the course of a study of the blood vessels and bile ducts of a large number of normal livers of man, by means of injection of celloidin and subsequent corrosion, we were struck by the frequency with which specimens of all types fell apart along a line joining the fossa for the gallbladder to the inferior vena cava, unless the main trunks had been thoroughly hardened before the specimen was handled. As this method is admirably suited to the demonstration of vascular distribution, it has been used to investigate the question more thoroughly. A series of livers from the human cadaver have been injected through the separate branches of the portal vein, hepatic artery and bile duct in order to study the constancy of the separation and its situation with regard to the three vessels. Thus the right and left branches of the portal vein, the right and left branches of the hepatic artery, and the right and left hepatic duct were injected with different colors four

21 Gilbert, A., and Villaret, M. *Recherches sur la circulation du lobule hépatique*, Arch de med exper et d'anat path **21** 373, 1909

22 Bauer, A. *L'indépendance des lobes du foie est hypothèse*, J de l'anat et de la physiol **45** 1, 1909

23 Bartlett, F. K., Corper, H. J., and Long, E. R. *The Independence of the Lobes of the Liver*, Am J Physiol **35** 36, 1914

tunes In all, twelve livers were examined in this way, and thirty other specimens showing various combinations of injections were studied for the purpose of determining the relationship between the various systems

METHOD EMPLOYED

The method was identical with that previously used and described by us for injecting the hepatic vascular and biliary systems, except that contrasting colors were used in the two sides²⁴ It is necessary to define clearly the limitations and possibilities of the method before discussing the results The thickness of the injection material is so arranged that it will penetrate into the finest arterioles and venules and smallest bile ducts The success of this can be determined by counting the number of branchings from the parent stem to the smallest radicle In the liver this number varies between five and six, as has been shown by Mall and others If possible, the sinusoids are not entered if they are a solid specimen is produced which is useless for study It is therefore understood that what follows is based on a study of the extrasinusoidal circulation of the liver In considering the question of a sinusoidal circulation across the median plane we used microscopic methods with tissue from normal livers and from the line of demarcation in cases of occlusion of single branches of the various vessels

RESULTS

Portal Vein—In all separate injections of the right and left branches of the portal vein with different colors, a striking and constant result was produced The right branch was found to be distributed over an area including that portion of the liver from the right extremity to a plane passing through the middle of the fossa for the gallbladder and the point of entrance of the hepatic veins into the inferior vena cava The left branch supplied the left half of the liver from this line of division to the left extremity (fig 1) The gallbladder lay in a cleft between the two sides, thus occupying a median position in the liver itself Its efferent veins usually drained into the right and left branches of the portal vein, although occasionally more into one than the other as these veins are large and anastomose freely over the surface of the vesicle, this arrangement varied considerably with the injection Contrary to the generally accepted view, it was usually found that two rammentales supplied the spigelian lobe, one arising from each branch of the portal vein The line of division thus practically always splits the spigelian lobe into two equal and longitudinal portions In order to

24 Counseller V S and McIndoe, A H Dilatation of the Bile Ducts (Hydrohepatosis), Surg Gynec Obst 43 729, 1926

examine this plane of separation more carefully and to make sure that no anastomotic branches crossed the median line, injections of single branches were made, with the result that each side was found to be an independent anatomic unit. The contiguous surfaces of the two sides were composed of tiny branches identical with those occurring on the outer surface of the organ. Many large branches could be seen coming

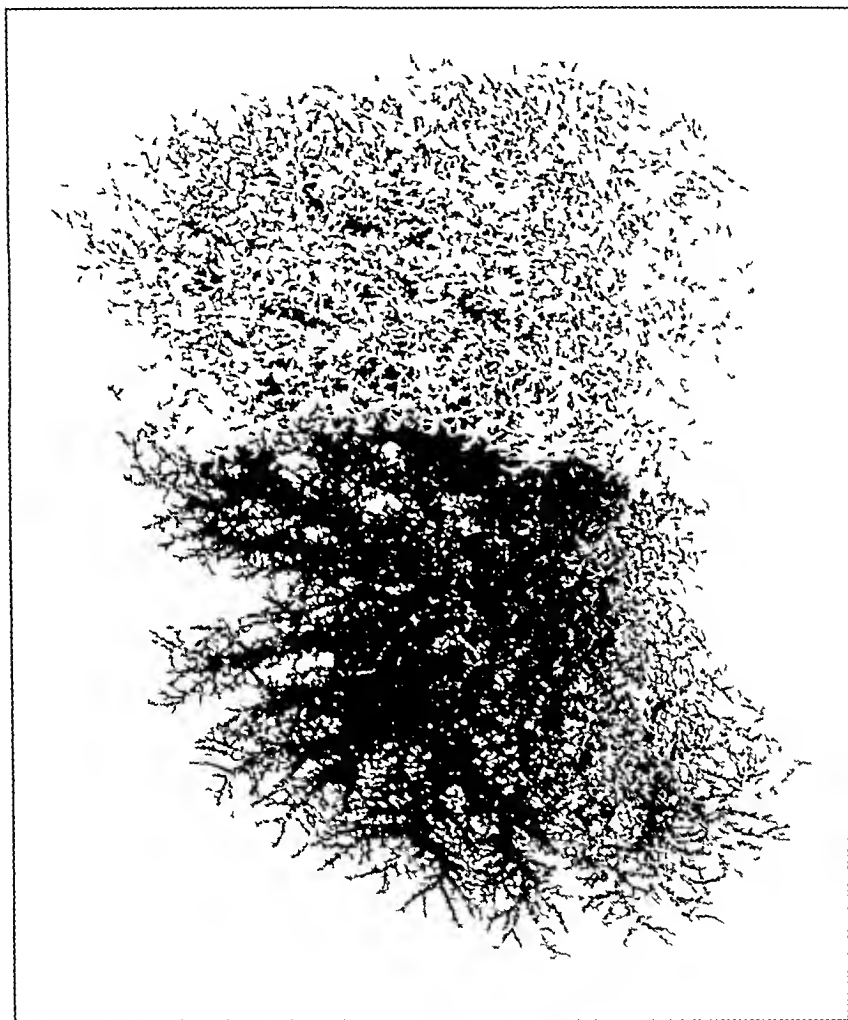


Fig 1—Injection of celloidin in the right and left branches of the portal vein. Note the relation of the line of separation and the fissure for the falciform ligament. Superior view.

to the surface and then turning aside, breaking up into a series of small veins in stellate fashion, as though they had suddenly encountered an invisible obstacle. No such clearly definite area existed in any other portion of the portal venous tree, the smaller radicles freely intermingled so as to make their separation practically impossible. This would effec-

tively dispose of the view that the line of separation represents merely the division between two portohepatic venous systems. The following scheme represents the named branches contained in the two main divisions

Right portal vein	{	Ramus arcuatus	
		Ramus cysticus	
		Ramus descendens	
		Right ramus omentalis	
Left portal vein	{	Left ramus omentalis	
		Ramus angularis	
		Recessus umbilicalis	{ Left arborization
			{ Right arborization

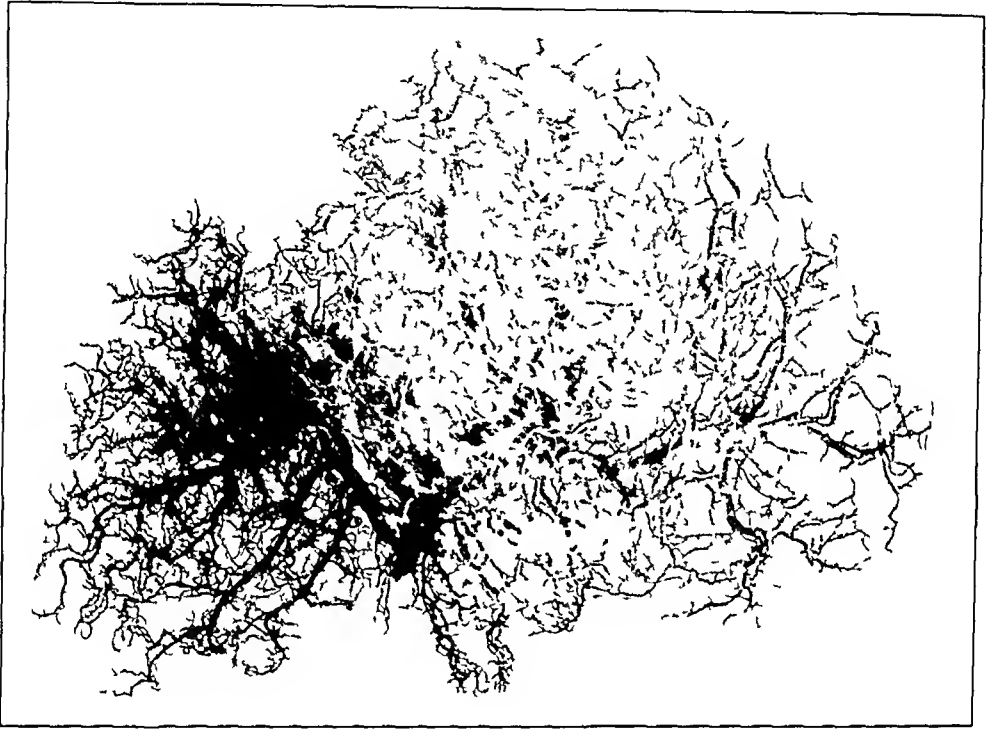


Fig 2—Injection of celloidin in the right and left branches of the hepatic artery. Superior view

As has been previously pointed out, however, many of these named branches are of no greater importance in point of size than unnamed ones that accompany them. The ramus angularis, for instance, is only one of the many large branches that supply the lateral portion of the left lobe. The ramus arcuatus and ramus descendens also are representative of groups rather than single channels. It seems, therefore, somewhat unwarranted to ascribe to them alone the rôle of blood channels to definite lobes of the liver, and to divide the organ anatomically on that basis.

Hepatic Artery—Here, too, it was possible to show a definite line of separation between the right and left branches corresponding entirely

in situation and characteristics to that in the portal vein (fig 2) In the four cases in which the two sides were injected, and in others in which combinations of artery-vein and artery-bile duct were made, the line of division was found to be constant, however, certain slight differences were noticeable In the portal vein the separation outside the sinusoidal circulation was found to be absolute, not even venule-sized trunks crossing the boundary In the artery, as has been noted, there was a marked tendency to an arteriolar anastomosis, both in the capsular plexus on the surface of the liver and in the vaginal plexus in the portal spaces It was therefore not surprising to find that a slight arteriolar anastomosis existed from side to side, sufficient to show a little mixing of the two colors It was most easily seen between the capsular vessels of the two sides, but even at its best the transference was slight As with the vein, each branch sent a twig to the spigelian lobe and then broke up into its terminal divisions, corresponding in distribution to those of the portal vein, with which they remained closely related

Bile Ducts—Injection of the right and left hepatic duct was rather more difficult to carry out because the point of division of the common hepatic duct is slightly higher in the hilum of the liver The passing of a ligature round the cannulas is extremely likely to rupture the hepatic tissue and damage the vasa aberrantia in this situation, with consequent leakage which is difficult to control With care, however, satisfactory specimens were obtained, which demonstrated beyond doubt that the biliary drainage of the liver is anatomically as distinctive as its vascular supply

Here again the line of demarcation coincided entirely with that described for the portal vein and hepatic artery (fig 3) Whatever pressure was employed, anastomosing branches could not be demonstrated between the two sides, even in specimens in which the fifth and sixth orders of branchings had been reached A slight transference occasionally took place in the cleft formed by the right and left hepatic ducts, by way of the vasa aberrantia, where, as is well known, a slight communication from side to side may occur by means of these vestigial structures This must be regarded as an extrahepatic site, and Kiernan and others²⁵ probably found that injection fluids pass from right to left by this route In order to show the complete absence of cross-anastomosing vessels more convincingly, a case of obstruction in the common duct by carcinoma of the head of the pancreas was chosen in which there was marked hydrohepatosis The two sides were injected sepa-

²⁵ Kiernan F The Anatomy and Physiology of the Liver, Phil Tr Roy Soc London, 1833, p 710

ately and at different times, but even with such huge dilatation as had occurred, no channels were opened between the two sides

Since the smaller branches of the bile ducts accompany the portal vein and hepatic artery, they will bear the same general relation to the hepatic parenchyma. When the portal vein, hepatic artery and bile ducts were injected simultaneously, the plane of separation of their right and left branches was common to all three (fig. 4)

To summarize. The liver is divided into two more or less equal parts by a line from the center of the fossa for the gallbladder to the

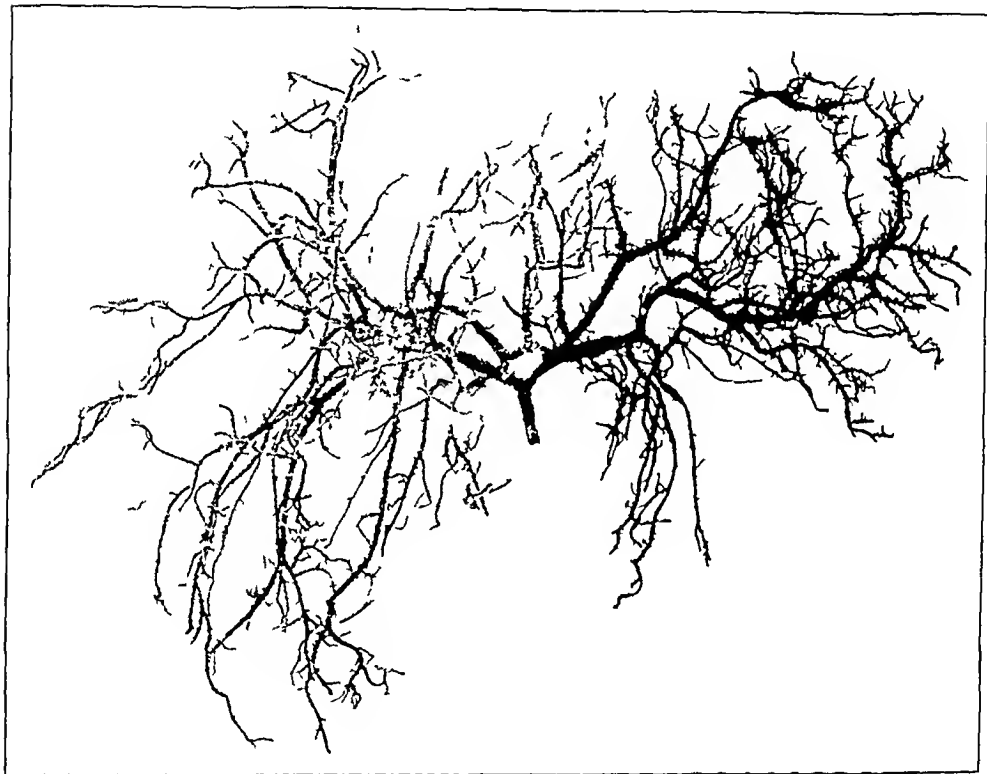


Fig. 3—Injection of celloidin in the right and left hepatic ducts in a normal liver

entrance of the hepatic veins into the inferior vena cava. Each half is supplied by a branch of the portal vein and hepatic artery, and drained by a branch of the bile duct. With regard to the portal vein, gross anastomosis does not occur between the two sides, only sinusoids crossing the median line. The two branches of the hepatic artery also respect the boundary line of the two lobes, but the division is not so absolute. Besides the capillary circulation, there is an arteriolar anastomosis from side to side, chiefly in the capsular and vaginal branches. The separation of the two bile ducts is absolute. While there may be an anastomosis between the bile canaliculi of the two sides, the bile ducts, per se, are entirely limited to their appropriate sides.

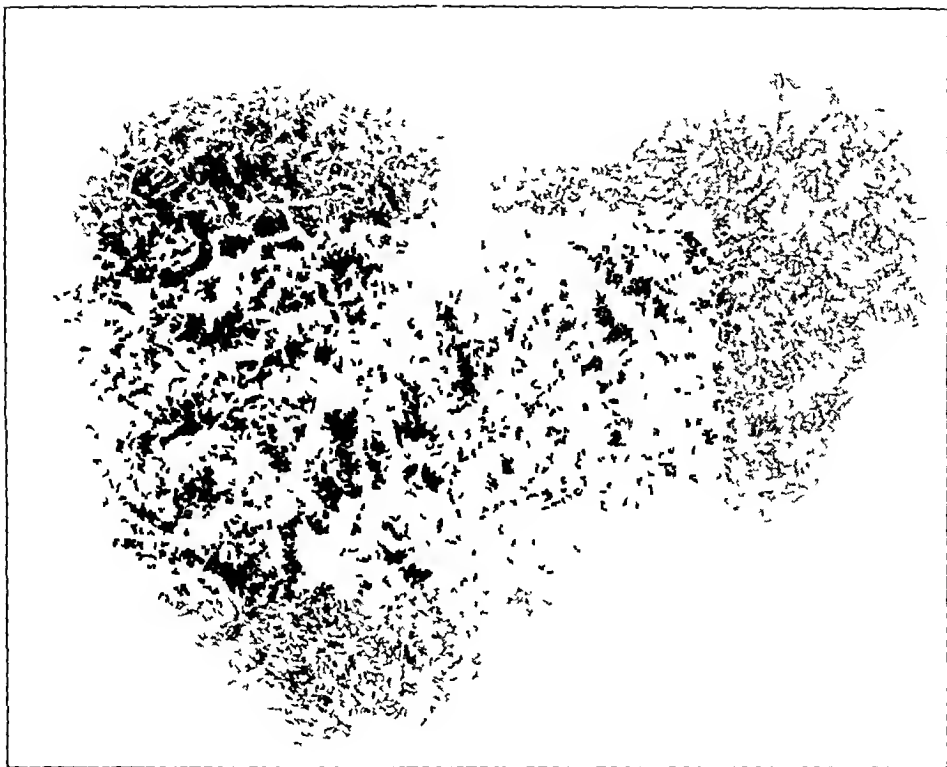


Fig 4—Injection of celloidin in portal vein, hepatic artery and bile ducts showing plane of separation common to all three vessels

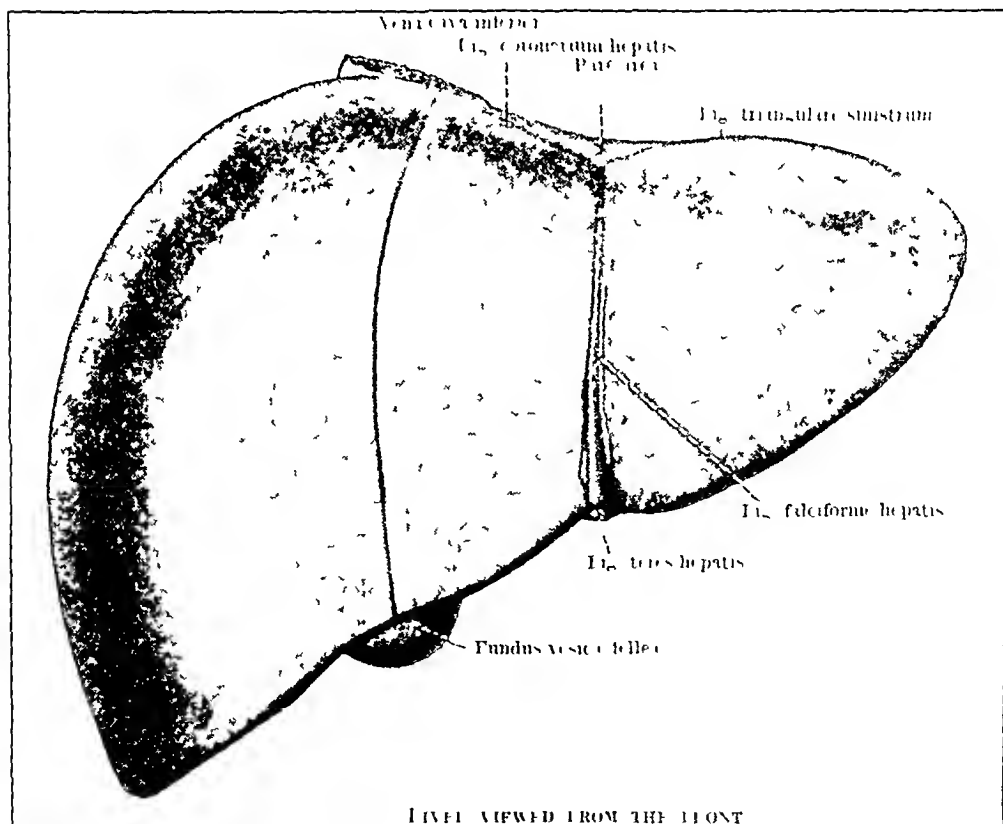


Fig 5—Surface markings of the plane of division, superior view (Cunningham)

SURFACE MARKINGS OF THE LOBES OF THE LIVER

The line bounding the plane of separation of the right and left lobes of the liver passes from the median point of the entrance of the hepatic veins into the inferior vena cava and straight across the superior surface of the organ to the middle of the notch for the gallbladder on the inferior margin. Occasionally there is a slight convexity to the right or left, though generally the line is direct (fig 5). On the inferior surface the line proceeds along the middle of the fossa for the gallbladder,

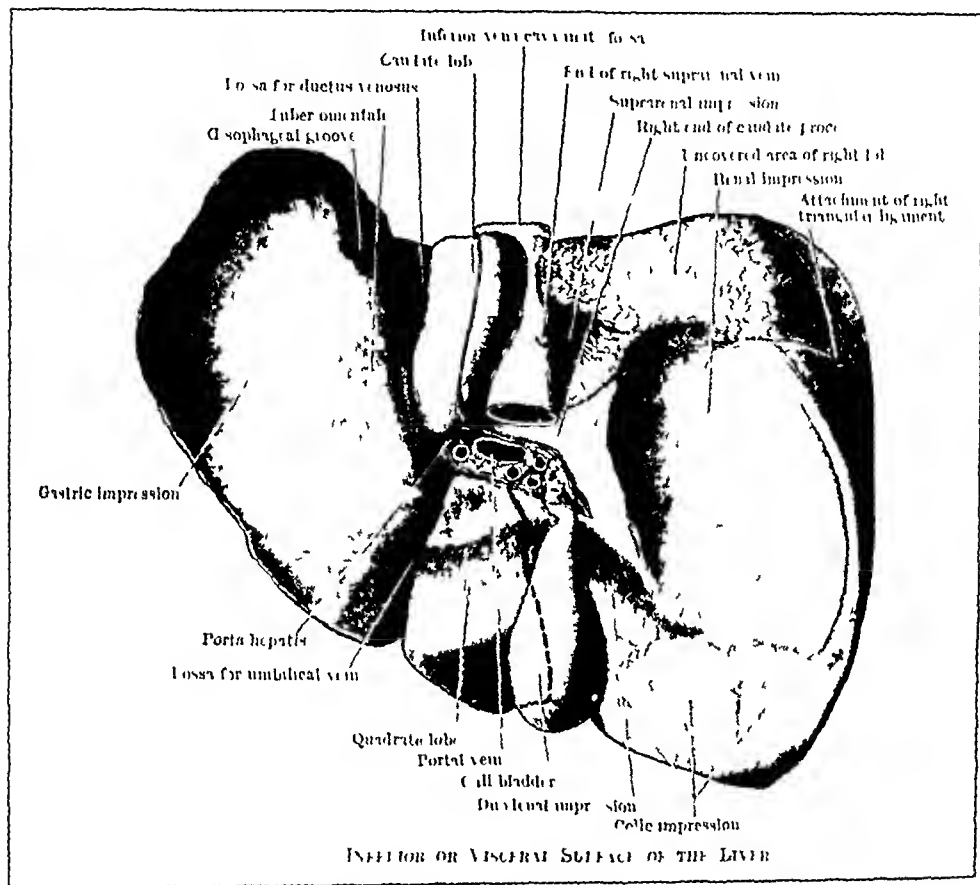


Fig 6—Surface markings of the plane of division, inferior view (Cunningham)

deviates a little to the left toward the porta hepatis, and then passes through the point of division of the three vessels at the hilum. It then runs toward the entrance of the hepatic veins into the inferior vena cava along the middle of the fossa for that structure, at the same time dividing the spigelian process longitudinally into halves (fig 6).

EVIDENCE FROM PATHOLOGIC LIVERS

We have demonstrated that there is at least a constant gross separation between the two sides of the liver. How completely autonomous the lobes may be anatomically and possibly functionally will depend

largely on the efficiency of a capillary anastomosis from side to side, if it occurs. If the blood supply and biliary drainage of each lobe is entirely limited to its own side, a unilateral occlusion of the separate branches should produce a lesion involving the whole lobe, clearly marked off from the opposite side along this plane of division. On the other hand, if the circulation across the median line is free, little or no effect is produced, but if slight overlapping occurs, there is partial compensation for the lesion. The effects of such lesions are fairly well known. Occlusion of either branch of the bile duct or hepatic artery invariably leads to atrophy and cirrhosis of the corresponding half of the liver,²⁶ in the first case, and to necrosis in the second. As Winternitz²⁷ has shown, occlusion of the portal vein may or may not be followed by infarction, depending on the pressure in the hepatic artery and the presence of stasis in the inferior vena cava. As a rule, little change is noted beyond slight congestion, although massive infarcts are sometimes produced.

The following three cases were selected as being representative of what may occur in various types of unilateral obstruction in the three vessels. In each case microscopic sections were taken from various points at the edge of the resultant lesions in order to demonstrate capillary anastomosis.

REPORT OF CASES

CASE 1—*Thrombosis of the right branch of the portal vein*

A woman, aged 56, was admitted to the hospital with signs of pneumonia in the left side of the chest and generalized abdominal tenderness, more marked in the upper right quadrant. For five days the patient made fair progress, but following the onset of severe diarrhea, rapidly became worse, and died on the eighteenth day. At necropsy the anatomic diagnosis was adenocarcinoma of the sigmoid without metastasis, subacute hemorrhage enteritis, thrombosis of the left branch of the portal vein with hemorrhagic infarction of the left half of the liver, cloudy swelling of the liver, spleen and kidneys, and congestion and edema of the lungs.

As the interest in this case lies in the liver, a description of the organ will be given. Its weight was 1,500 Gm. Beneath the capsule on the superior surface, a sharply defined line of demarcation ran from the gallbladder notch over the dome of the organ to the region of the entrance of the hepatic veins into the inferior vena cava. The right side was composed of normal brownish-yellow

26 Behrend, M. Experimental Ligation of the Hepatic Artery. A Preliminary Note, *Surg Gynec Obst* **31** 182, 1920. Narath, A. Ueber die Unterbindung der Arteria hepatica, *Beitr z klin Chir* **65** 504, 1909, Ueber Entstehung der anamischen Lebernekrose nach Unterbindung der Arteria hepatica und ihre Verhütung durch arterioportale Anastomose, *Deutsche Ztschr f Chir* **135** 305, 1916. Staehlin, Edward. A Contribution to the Study of Blood Supply of the Liver, *Surg Gynec Obst* **11** 479, 1910.

27 Winternitz, M. C. The Effect of Occlusion of the Various Hepatic Vessels Upon the Liver, *Bull Johns Hopkins Hosp* **22** 396, 1911.

hepatic tissue, while the left presented a uniformly hemorrhagic surface, with obliterated lobular markings, and marked softening as compared with the right side. On passing the finger from one side to the other the line of demarcation was more readily perceived. After section, the right lobe appeared practically normal, except for a little swelling and indistinctness of the lobular markings. On the left side the lobules were shrunken, and almost indistinguishable, with dark red congested centers and slightly lighter peripheral zones (fig 7). Dark blood could be freely expressed from the cut surface. The left branch of the portal vein was completely occluded by an antemortem clot which extended into several of its smaller branches. The hepatic artery on both sides and the right branch of the portal vein were free.

Microscopic examination of the right lobe showed cells apparently fairly normal in structure and arrangement. Sections from the left lobe showed almost complete atrophy of the hepatic cell columns, most marked at the centers of the

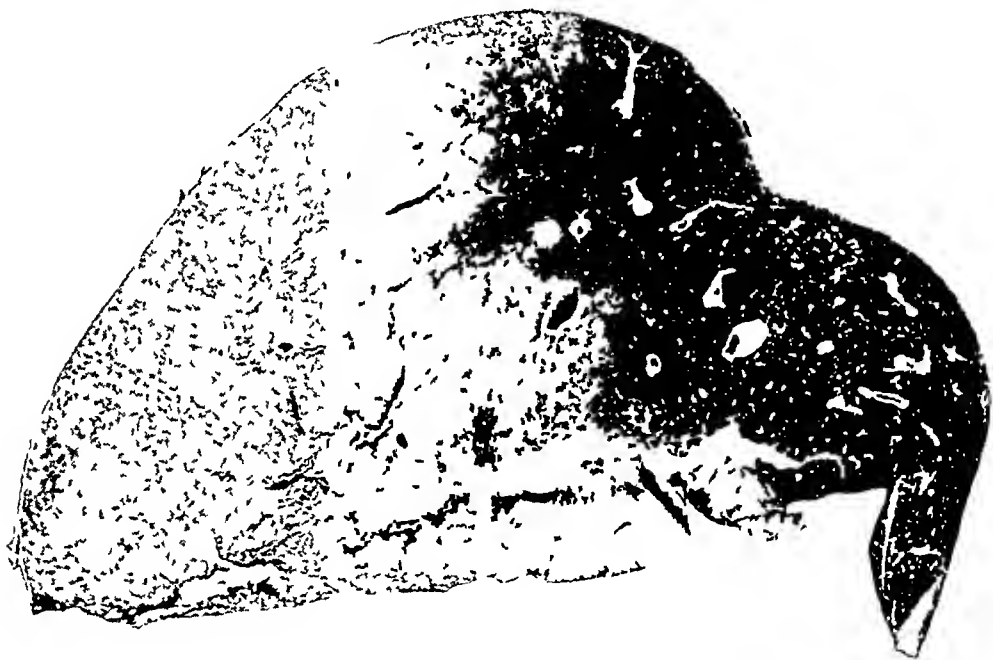


Fig 7—Thrombosis of the left branch of the portal vein with infarction of the left lobe of the liver. The edge of the lesion represents the true line of separation between the right and left lobes.

lobules, and slightly less in degree at the periphery. The sinusoids were hugely dilated with blood and contained many polymorphonuclear leukocytes. Sections from the edge of the lesions showed normal tissue on the right, and on the left an abrupt transition to the condition just described. It could be clearly seen, however, that many normal capillaries communicated from normal to abnormal tissue, indicating that while an anastomosis occurred, it was insufficient to compensate for the vascular occlusion on the left side. This plane of demarcation corresponded entirely to that which we have described as separating the right and left lobes of the normal liver.

CASE 2—Obstruction of the left hepatic duct

A woman, aged 56, was admitted to the Mayo Clinic complaining of intermittent attacks of severe epigastric pain radiating to the right shoulder blade and associated with nausea and vomiting of fifteen months' duration. On examina-

possible in how far our thesis is in harmony with them. For the facts concerning the embryology of the liver we have drawn freely from the textbooks of Keibel and Mall,²⁸ Bailey and Miller,²⁹ Kollman,³⁰ Hertwig,³¹ Minot,³² and Prentiss and Arey.³³ Stress has been laid on certain points since they are believed to have more importance than has hitherto been accorded them.

The liver develops as a diverticulum from the central portion of the future duodenum and invades the median sagittal portion of the septum transversum, or that part of it known as the ventral mesentery. Before mammalian embryos had been satisfactorily studied, it was known that in the chick the liver arose from two intestinal outgrowths, so that a similar development was predicted for mammals. Although a bilateral origin has been described in some invertebrates, it has not been found in man.³⁴ In the 4 mm embryo the already substantial mass of liver cords is found to be growing actively into the mesenchyme of the ventral mesentery, and to be approaching the paired system of vitelline and umbilical veins which forms a remarkably constant ground-plan in this region. At this time, and coincident with the proliferating hepatic mass, the branches of the omphalomesenteric (vitelline) veins are forming plexuses within the mesentery. The result is that when the liver anlage in its dorsal course comes into contact with the vitelline veins, they invaginate one another, so that the cords of liver cells are closely invested with endothelium, and the venous channels form an intricate network of sinusoids about them (Minot). The primitive liver at this stage forms into incompletely separated halves, the right and left wings (Lewis),³⁵ or the right and left dorsolateral lobes (Bailey and Miller), in relation to the two vitelline veins. Thus, before the umbilical veins have become incorporated into the liver, two well recognized subdivisions have occurred in relation to the future portal vein. This is the first and only evidence of true embryologic lobes in the development of the organ.

28 Keibel, F., and Mall, F. P. *A Manual of Human Embryology*, Philadelphia: J. B. Lippincott and Company, 2: 403, 1912.

29 Bailey, F. R., and Miller, A. M. *Textbook of Embryology*, ed. 4, New York: William Wood and Company, 1923, p. 316.

30 Kollman, J. *Handatlas der Entwicklungsgeschichte des Menschen*, Jena, Gustav Fischer 2: figs. 382, 383, 385, 1907.

31 Hertwig, Oscar. *Handbuch der vergleichenden und experimentellen Entwicklungslehre der Wirbeltiere*, Jena: Gustav Fischer 2: 139, 1905, pt. 2.

32 Minot, C. S. *A Laboratory Textbook of Embryology*, Philadelphia: P. Blakiston's Son and Company, 1903, p. 100.

33 Prentiss, C. W., and Arey, L. B. *A Laboratory Manual and Textbook of Embryology*, ed. 3, Philadelphia: W. B. Saunders Company, 1922, p. 176.

34 Scammon, R. E. *The Development of the Elasmobranch Liver*. I. The Early Development of the Liver. II. The Development of the Liver Ducts and Gallbladder. *Am. J. Anat.* 14: 333, 1912.

35 Lewis, F. T., quoted by Keibel and Mall (footnote 28).

In the 6.5 mm embryo the extrahepatic portions of the two vitelline veins have anastomosed both ventrally and dorsally to the primitive duodenum to form two venous rings with three cross connections between them. By atrophy of the right side of the caudal of the two vitelline loops and the left side of the cranial one, an S-shaped course is pursued by a common vitelline trunk, composed mostly of the left vein but partly of the right, to reach the liver at the site of the former right vitelline vein. This in turn opens into the cranial anastomosis which now becomes intrahepatic. Thus the extrahepatic portion of the future portal vein is formed. Except that the liver is now supplied by a single trunk, the two intrahepatic omphalomesenteric (vitelline) plexuses retain their relationships undisturbed with the right and left dorsolateral lobes.

When the umbilical veins gain their connections with the liver sinusoids, there is a radical though temporary change in the arrangement of the venous plexuses. The right umbilical vein disappears completely early in the development. The umbilical blood is now poured into the cranial anastomosis of vitelline veins by way of the left umbilical vein, and subsequently develops a new path, the ductus venosus, to the right horn of the sinus venosus. The main factors in the formation of this pathway and its obliquity are the sudden accession in size of the right side of the liver and the consequent circuitous course taken by the right vitelline vein. Thus in the 7 mm embryo, as has been stated, the entire right umbilical vein and caudal portion of the right vitelline are absent, leaving intact the common vitelline and intrahepatic portions of both vitellines forming the definitive portal vein, and in addition, the newly incorporated left umbilical vein. During the further development of the liver the left umbilical vein completely overshadows the vitelline. With the redirection of the blood flow obliquely across the liver from left to right, and the bulging of the organ on each side of the relatively broad attachment of the ventral mesentery to the diaphragm, the future falciform ligament, two new or secondary right and left lobes, have been generally recognized. The separation is rendered still more convenient by the fact that the falciform ligament and its contained vein, once a left lateral structure, now moves toward the median plane, while the gallbladder, which is without doubt morphologically median (Lewis), is found on the right.

At birth, however, a further series of changes occurs which obliterates all active traces of the umbilical circulation and restores the vitelline or portal vessels to their former importance. The ductus venosus and the umbilical vein become fibrous cords, and the whole blood supply of the organ is once more diverted through portal channels.

To return to the embryo of 6.5 mm, it is found that the hepatic duct consists of a single solid cord of cells joining the hepatic mass to

the common duct, and so to the duodenum. At 10 mm it receives a right and a left branch from the right and left lobes. Within the liver the larger ducts cannot be traced farther, nor is it clear whether they are outgrowths of the hepatic duct or whether they arise in situ by a transformation of the cells of the hepatic parenchyma. The smaller periportal branches do not appear until much later (22.8 mm), and they apparently spread along the branches of the portal vein, acquiring a lumen and communicating with the parenchyma as they go. At the same time as the hepatic duct forms a single cord the hepatic artery can be traced to it. At 22.8 mm the artery extends along the cystic and hepatic ducts, the former branch being much larger, owing to the earlier appearance of the gallbladder. Following the development of mesenchyme around the hepatic duct and portal vein, ramifications of the artery appear within it in close association with the two vessels throughout their course. The important point with regard to both the ducts and the artery is that they are of much later development than the vein, and their disposition within the liver is embryologically determined by the arrangement of the portal vessels, and hence of the vitelline circulation.

If this account of the development of the liver is true, one should expect to find that in the adult, the right and left branches of the portal vein regularly supply the true embryologic right and left lobes of the liver, and that the bile ducts and hepatic artery agree in their distribution with the portal vein.

Our experiments show clearly that the liver of man is constantly and regularly divided into halves, according to the distribution of the portal vein, by a plane passing through the fossa for the gallbladder and the entrance of the hepatic veins into the inferior vena cava. This separation is always followed by the bile ducts and hepatic artery. It would seem, therefore, that, just as in the embryo the true plane of embryologic division is admitted to lie between the right and left omphalomesenteric veins, the only absolute and definite subdivision of the adult organ lies in this constant separation of the three vessels, the principal member of which represents the two fetal veins. The falciform ligament is of secondary importance. Under these circumstances it may be asserted with Cantlie that the liver is a bilaterally symmetrical organ, with the gallbladder as its morphologic center. The truth of this may easily be verified by sectioning the liver along the line as described and observing the total absence of portal veins, bile ducts and arteries on the two cut surfaces. Moreover, the two portions are almost equal in weight, the difference rarely being more than 100 Gm.

As the line of division between the true right and left lobes is unmarked by any fissure, unless it is by the fossa for the gallbladder and

an occasional partial or complete bifid spigelian lobe, it is necessary to explain the presence of fissures and apparent lobes on some other basis than that supplied by a single developmental cause. It is well known that in comparison with lower animals, the liver of man shows surprisingly few fissures or well marked lobulations. Comparative anatomists have noted many similarities, but, again, in such closely related species as *Gorilla gorilla*, inexplicable anomalies are found. Among the widely divergent reasons given by anthropologists for these dissimilarities are the character of the food, the configuration of the stomach and diaphragm, the position of the animal—whether erect or prone—the disposition of the fetal veins and in general the molding effect of the other abdominal organs. Harris³⁶ further suggests that the changes occurring in the normal physiologic umbilical hernia may yield the answer to this puzzling question. On one point the embryologist and the morphologist are agreed, namely, on the profound influence which pressure, both from intra-abdominal organs and from fetal structures, plays in the external form of the organ. Toldt and Zuckerkandl³⁷ have demonstrated the tremendous changes in shape which the liver undergoes from fetal to adult life. Atrophy in one situation is followed by hypertrophy in another, so that the organ is in a constant state of parenchymal movement. They attribute these changes solely to extra-hepatic pressure. Definite traces of such alterations may clearly be seen in the coronary ligaments, especially on the left side, in the angle between the right and left hepatic ducts, in the transverse fissure and in the membranous bridge which unites the spigelian process with the right lobe behind the inferior vena cava. Here bile ducts, veins and arteries, preserving their hepatic relationships, are found stranded in fibrous tissue. Mall, who confirms these observations, points out that the distribution of the portal blood to the hepatic parenchyma is remarkably even, no region being especially favored, so that any enduring local irregularity would produce a shift of parenchyma. While these influences are normally constant and produce a uniformly shaped liver, the variations in form, such as have been recorded in man by Ruge and Cullen,³⁸ are remarkable. It is commonly known that the liver may be greatly deformed by thoracic or abdominal tumors, by collections of fluid or by external influences, such as tight lacing. More recently Rous and

36 Harris, H. A. Intrapelvic Ectopic Testis Combined with Ectopia Vesicae Congenital Umbilical Hernia and Abnormal Gallbladder, *Arch Surg* **13** 644 (Nov.) 1926

37 Toldt, C., and Zuckerkandl, E. Ueber die Form und Texturveränderungen der menschlichen Leber während des Wachstums, *Sitzungsbd. d. Akad. d. Wissensch* **72** 24, 1876

38 Cullen, T. S. Accessory Lobes of the Liver. An Accessory Hepatic Lobe Springing from the Surface of the Gallbladder, *Arch Surg* **11** 718 (Nov.) 1925

Larimore³⁹ have shown how changes in the intrahepatic pressure relationships from local conditions may effect the shape of the organ

The mutilobed liver of Rex, Mall and Flower, considered in relation to the smaller branches of the portal vein, is, as Bradley states, probably more of descriptive value than of morphologic significance. It is clearly absurd to dignify the slight eminence between the gallbladder and the falciform ligament as a distinct lobe, and more so to accord to it an independent blood supply. In our vascular injections we have always found that the branches named which supply these areas course along with others just as large and important, and that there is little specificity at such a distance from the portal trunk. The spigelian lobe has at least two main branches dividing it into two parts, one from each main branch of the portal vein, so that morphologically half the spigelian lobe belongs to the true right lobe and half to the left. Beyond the two principal lobes, there can therefore be little value in such minor subdivisions.

If it is admitted that the falciform ligament is a useful surgical landmark, there are certain practical objections to the assumption that it represents the line of division between the right and left lobes. These are concerned with the questions of atrophy and hypertrophy with unilateral lesions of the liver, with the dual portal current and with the possible functional independence of the two sides. A comparison of the relative positions of the falciform ligament and the true lobar boundary will convince one that the situation of the former is by no means constant. Sometimes it is nearer to the left side, sometimes nearer to the right. An accurate estimation of the amount of atrophy or hypertrophy, or even a demonstration of its presence, may thus be impossible, unless the true dividing line between the two sides is kept in mind. On the other hand, such changes have undoubtedly been reported when in reality the liver was entirely normal. The alterations resulting from local disturbance of the portal or hepatic blood supply or of biliary drainage are analogous to the parenchymal shifting of the fetal liver. From whatever cause hypertrophy occurs, it is usually regarded as a compensatory phenomenon similar to the overgrowth of other glandular organs which occurs when they are forced to carry added functional burdens. The possibility of atrophy in one lobe essentially dependent on a similarly developing hypertrophy elsewhere does not seem to have been fully appreciated in the study of the pathologic changes of the liver. Rous and Larimore have recently shown that if the right portal vein is ligated, atrophy occurs in the right lobe with a compensatory hypertrophy of the left. If, however, the bile duct from the proliferating side is occluded and the hypertrophy checked, atrophy does not occur on the

39 Rous, Peyton, and Larimore, L. D. Relation of the Portal Blood to Liver Maintenance. *J. Exper. Med.* **31**: 609. 1920

right side Little attention has been paid to this question of conditional hypertrophy It may well explain the advanced local atrophy found in livers containing an echinococcus cyst, a gumma, a slow growing tumor or other limited process causing pressure on portal radicles Such portal diversion may also account for the extreme atrophy and hypertrophy met with in the so-called *hepar lobatum* We have noted that, following long-continued obstruction of the common duct, there is distinct atrophy of the left lobe, due to the greater constricting effect of the dilated left bile duct on the longer and more slender left portal vein Correspondingly, there is a more severe grade of hydrohepatosis in the left lobe These differences are slight and can be detected only by careful observation of the relative sizes of the true right and left lobes Microscopic examination may reveal no sign of their presence, for, as McCallum⁴⁰ has shown, large areas of hepatic tissue may disappear without the least replacement of connective tissue

We do not intend to dwell on unilateral lesions of the liver, associated as they are with the controversial question of the dual portal current It is sufficient that many interesting avenues for investigation are opened up From the pathologic point of view, there is much evidence that the mesenteric and splenic circulations are destined for definite areas of the liver The astonishing predilection of amebic abscess for the right lobe, the frequency with which parenchymatous degeneration of the same area occurs in cases of peritonitis and diseases of the intestines (Wassink)⁴¹ and the occasional localization of metastatic carcinoma in one or the other lobe point toward this autonomy There are at least excellent anatomic reasons why such things should occur Whether the right and left lobes are functionally independent is another question which requires further investigation, and which is entirely beyond the scope of the present paper

CONCLUSIONS

- 1 The right and left branches of the portal vein are regularly and definitely divided along a line from the fossa for the gallbladder to the entrance of the hepatic veins into the inferior vena cava Except for the intercellular sinusoids, which are probably insufficient to maintain a collateral circulation, there is no gross anastomosis across the line of separation

- 2 The right and left branches of the hepatic artery are also separated in the same manner and at the same situation There is an arteriolar

40 McCallum, W C A Textbook of Pathology, ed 3 Philadelphia W B Saunders Company 1924 p 63

41 Wassink, W F Unilateral Degeneration of the Liver Caused by Division of the Portal Circulation *Nederl Tijdschr v Geneesk* 1915 p 2145

anastomosis between the right and left sides chiefly between the capsular and vaginal branches, but it is not sufficient to prevent infarction of the corresponding lobe following occlusion of either branch

3 The line of separation of the right and left hepatic ducts is identical with that of the artery and vein, but the division is absolute

4 The facts of embryology, anatomy and pathology are in accord with the assumption that the two areas of liver determined by this division, which is common to the three vessels, represent the true embryologic right and left hepatic lobes and that the falciform ligament is merely an arbitrary landmark

SPONTANEOUS GANGRENE OF THE EXTREMITIES

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During the past few years lesions affecting the blood vessels of the extremities have been well differentiated and the clinical syndromes associated with them have become well recognized. It may be said, however, without much fear of contradiction, that most things concerning the etiology of the changes in the vessels leading to spontaneous gangrene and many things concerning the results of these are still in a state of distressing uncertainty.

Clinically, spontaneous gangrene occurs in the old and in the relatively young, thus justifying the clinical classification of senile and pre-senile gangrene. These are dependent on entirely different processes, one degenerative in character, and the other inflammatory—an arteritis or, because of the almost constantly associated involvement of veins, a thrombo-angitis.

According to Maichand, the term arteriosclerosis includes all those changes occurring in an artery which lead to a thickening especially of the intima, to degenerative changes (fatty degeneration), to sclerosis and calcification (including calcification of the media), and also to inflammatory and productive processes.

Clinicians and pathologists have different criteria regarding arteriosclerosis. To the clinician, arteriosclerosis indicates a rigid, noncompressible, pipestem-like artery. The pathologist, on the other hand, is concerned mostly with the earlier changes of proliferation, followed by degeneration or the reverse. It is generally admitted that in arteriosclerosis the principal changes occur in the media. In advanced cases the adventitia may also be affected. There is no unanimity of opinion, however, concerning the sequence of these changes. While some regard the changes in the media and internal elastic lamina as primary and those in the intima as secondary, others hold the opposite view. These differences of opinion may be due in part to variability in the arrangement of the musculature and elastic tissue in different parts of the arterial tree.

The changes associated with presenile gangrene are definite. There is some confusion, however, in nomenclature, because of the terms which have been introduced. In 1879, von Winiwarter published pathologic observations of cases in which practically all the arteries of the leg were obliterated by a chronic proliferative process originating apparently in the intima. He gave the name of endarteritis obliterans to this process. This lesion undoubtedly is the same as that now known

as thrombo-angitis obliterans, characterized by an inflammation of the walls of the vessels, associated with thrombus formation, with subsequent vascularization, canalization and organization of the thrombus

Pathologically, arteriosclerosis and thrombo-angitis are distinct. The term endarteritis obliterans probably might be discarded to advantage. It has, however, the influence of long usage. In thrombo-angitis, arteritis and peri-arteritis (phlebitis and periphlebitis) are the initial lesions. In the evolution of the disease, healing is the rule, the products of the inflammatory stage being replaced by fibrous tissue.



Fig 1—Normal pattern of the arterial tree of the foot

In the series on which this study is based are 139 cases of spontaneous gangrene of the extremities, the records of which are complete enough to be accepted. There are forty-seven cases of arteriosclerotic gangrene, forty-three cases of arteriosclerotic gangrene associated with glycosuria, twenty-seven cases of gangrene occurring in diabetic patients in which the arterial changes, at present, were not pronounced enough to attract attention, fourteen cases of thrombo-angitis obliterans, one case of scleroderma, and seven cases in which arterial changes may have been a contributing factor in the gangrene, but infection played the principal part.

ARTERIOSCLEROTIC GANGRENE

The clinical phenomena associated with arteriosclerotic gangrene and thrombo-angitis are so well known that there is but little need for their consideration. I will quote, however, from the original description of Pott concerning the onset and progress of arteriosclerotic gangrene which appeared in his "Surgery," vol 2, published in 1819, in a chapter entitled "Observations on the Mortification of Toes and Feet." In this appears the following

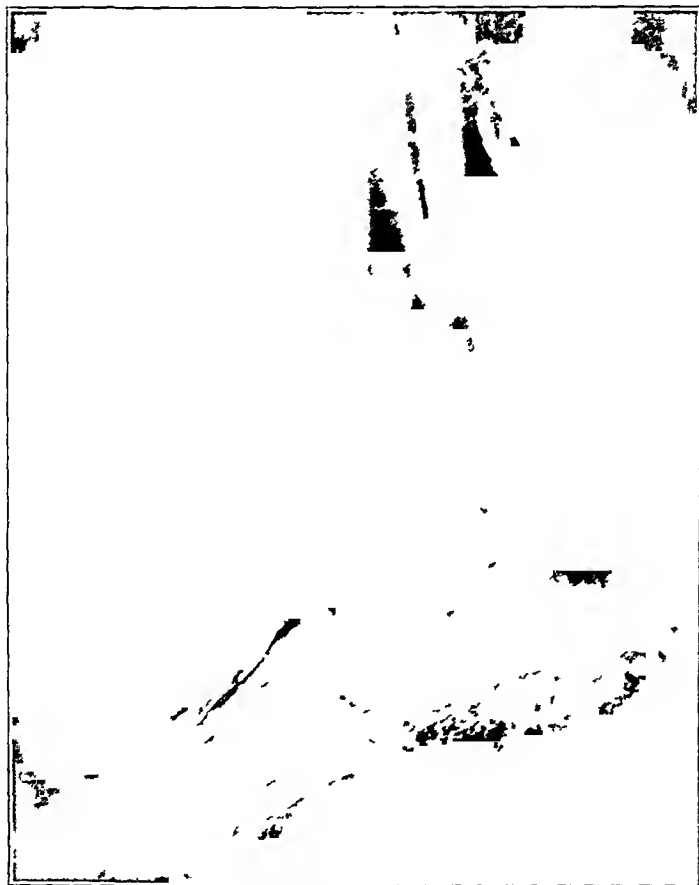


Fig 2—Injected specimen of leg and foot removed for arteriosclerotic gangrene showing imperfect filling of the vessels, occlusion of the main trunks and lack of collateral circulation

The powers and virtues of Peruvian bark are known to almost every practitioner of physic and surgery. Among the many cases in which its merit is particularly and justly celebrated, are the distempers called gangrene and mortification: its general power of stopping the one, and resisting the other, has made no inconsiderable addition to the success of the chirurgic art; but still there is a particular species even of these in which this noble medicine most frequently fails. I mean that particular kind, which, beginning at the extremity of one or more small toes, does, in more or less time, pass on to the foot or ankle, sometimes to a part of the leg; and in spite of all the aid of physic or surgery most commonly destroys the patient.

It is very unlike to the mortification from inflammation, to that from external cold, from ligature or bandage, or to that which proceeds from any known cause, and this as well in its attack as in its progress. In some few instances it may make its appearance with little or no pain, but in much the majority of cases the patient feels great uneasiness through the whole foot and joint of the ankle, particularly in the night, even before there is any other than a small discolored spot on the end of one of the toes.

It generally makes its appearance on the inside or at the extremity of one of the smaller toes by a small black or bluish spot, from this spot the cuticle is always found to be detached and the skin under it of a dark red color.

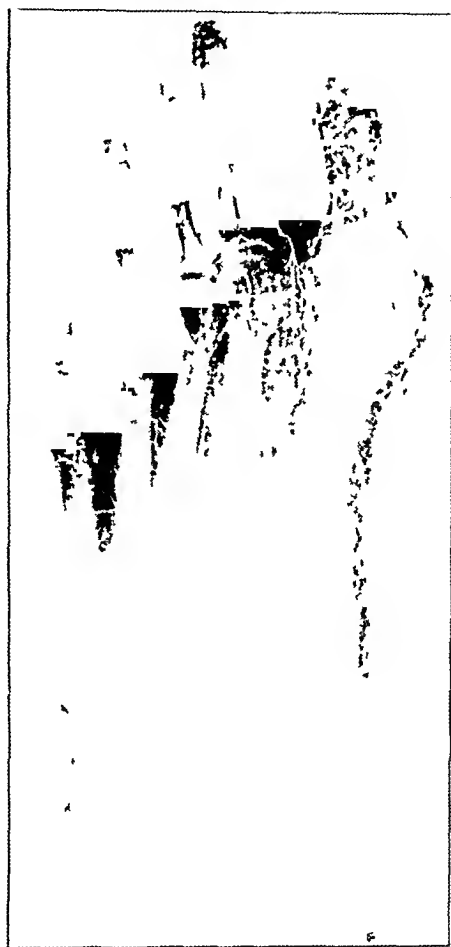


Fig. 3—Injected specimen of foot removed for arteriosclerotic gangrene, some collateral circulation seems to have developed, but it is small in amount.

If the patient has lately cut his nails or corns, it is most frequently, though very unjustly, set to the account of such operation.

Its progress in different subjects, and under different circumstances, is different. In some it is slow and long in passing from toe to toe, and from thence to the foot and ankle, in others its progress is rapid and horribly painful. It generally begins on the inside of each small toe before it is visible either on its under or upper part, and when it makes its attack on the foot, the upper part of it shows first the distempered state, by tumefaction, change in color and sometimes by

vesication, but wherever it is, one of the first marks of it is a separation or detachment of the skin

This clinical description of senile or arteriosclerotic gangrene is so accurate that nothing can be added. The question arises at once why gangrene is not observed more frequently in the upper extremity in arteriosclerosis. Pott's original description concerns itself with the toes and feet. But in the cases of arteriosclerotic gangrene of the feet the changes may be as advanced or more so in the vessels of the upper extremity.

One must be impressed with the frequency with which pulsation cannot be felt in either the *dorsalis pedis* or the posterior tibial arteries and still no evidence of a circulatory disturbance be evident and no symptoms except some fatigue or pain on exertion.

The arrangement of vessels in the lower extremity may determine the more frequent occurrence of gangrene in the lower than in the upper extremity. Not enough attention has been paid to the extent or location of the thrombus or occlusion. Embolism or thrombosis of the popliteal artery is practically always followed by gangrene. Heidenhain was one of the first to suggest that gangrene of this type was due to occlusion of the popliteal arteries or its branches. In eleven of the twenty cases examined by him, occlusion of the larger vessels—popliteal anterior and posterior tibials—by thrombi, in some cases organized, was found. An examination of statistics would indicate that in 50 per cent of the cases of senile gangrene the large vessels of the extremity are occluded. Occlusion of the popliteal artery by a recent thrombus is found in cases in which the gangrene is limited to a single toe. The possibility of a collateral circulation in these cases will be discussed after thrombo-angitis is considered.

Nine deaths occurred in the forty-seven cases of senile gangrene, a mortality of a little over 19 per cent. Three of the patients died of pneumonia, three of embolism and two of myocarditis. The cause of death in one case is not stated. Twenty-seven patients left the hospital with wounds healed. The wounds of the remaining twenty were granulating, but they healed subsequently.

It has been impossible to follow these cases to determine the length of life after amputation for senile gangrene, for in Baltimore one deals with a floating population, in which a thorough follow-up is difficult.

In two of the cases, gangrene developed in the remaining foot, in one almost nine years after the first amputation, and in the other almost four years later. In the first of these a recent thrombus was found in the popliteal artery when amputation was performed. This extended some distance up into the femoral artery.

Amputation through the condyles—Cairden's transcondylar amputation—is satisfactory in these cases. It is of interest to note, however, that in a considerable number of cases the incision may open after removal of the stitches, necessitating traction on the skin by adhesive strips in order to cover the stump. Death is not frequently caused by the operation, but is due to extension of the vascular disease or a terminal infection.

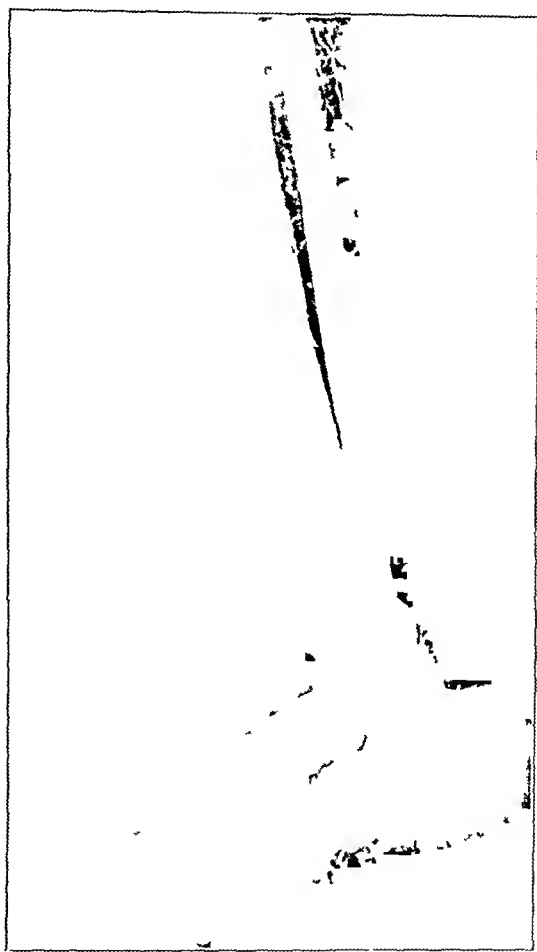


Fig. 4—Foot and leg injected after removal for arteriosclerotic gangrene, vessels difficult to inject, collateral circulation not developed, recent thrombus found in popliteal artery.

ARTERIOSCLEROTIC GANGRENE WITH GLYCOSURIA
(DIABETIC GANGRENE)

Since attention was first called to the not infrequent association of diabetes and gangrene by Marshall di Calvi, the relationship between the two has been studied frequently. That hyperglycemia with the associated metabolic changes is not alone the predisposing factor to gangrene has been conclusively demonstrated, for the severest form of diabetes

running a rapid course and terminating fatally, as well as the more chronic cases, with a marked hyperglycemia, may not present gangrene. It is probable that one errs as much in the opposite direction if one regards the glycosuria observed in so many of these cases as merely due to an arteriosclerosis involving the pancreatic vessels and denies a direct etiologic relationship between the hyperglycemia and the gangrene.

Arterial changes are common in patients with diabetes. Grube found vascular changes in sixty-six of seventy-seven diabetic patients and von



Fig 5—Foot and leg in case of intermittent claudication, showing arteriosclerosis of the main vessels, the dorsalis pedis and posterior tibial pulses are lacking, but this patient had no evidence of circulatory disturbance other than the intermittent claudication.

Noorden in 200 of 650 (30 per cent). Eliason and Wright have recently directed attention to this relationship. Arteriosclerosis was present in 66.6 per cent of their cases of gangrene occurring in diabetic patients. In nineteen cases it was not mentioned. Some of these cases dated back to 1903, and it was impossible to secure accurate data. They make the following statement concerning the association of the two

Inasmuch as gangrene in diabetics occurs about five years earlier than in senile arteriosclerosis and 66.6 per cent of the cases in which the condition of the arteries was recorded, showed arteriosclerosis and 100 per cent of all pathological and x-ray examinations showed it to be present, it would appear that there cannot be any question but that the local arterial condition plays an important part in the causation of gangrene of the extremities in diabetic patients and is therefore quite analogous in this respect to the senile form of gangrene.

Accumulating evidence indicates that the so-called diabetic gangrene is due to arteriosclerosis. It is dependent primarily on the same causes as arteriosclerotic gangrene, but is complicated by hyperglycemia. The study of the series herein considered shows that gangrene develops in the diabetic patient about a decade earlier than in patients with uncomplicated arteriosclerosis. The average age at which gangrene appears in the diabetic patient is 54.4 years, while the average at which senile gangrene appears is 66.2 years. Eliason and Wright state that arteriosclerotic gangrene associated with diabetes shortens life a full decade more than arteriosclerotic gangrene alone.

In the series occurring at Johns Hopkins Hospital in diabetic patients, there were forty-three cases of gangrene with marked arterial changes, and twenty-seven cases in which arteriosclerosis was not pronounced enough to attract attention or in which no particular attention was paid to the arterial lesion. Arteriosclerosis was therefore noted in 61.4 per cent of the cases, a percentage which corresponds closely to that of other statistics. Eighteen, or 25.7 per cent, of these patients died as the direct result of the gangrene. Death was ascribed to diabetic coma, pulmonary embolism, shock following operation in one case, lobular pneumonia, ulcerative colitis and advancing gangrene, gangrene of both feet being observed in one case.

THROMBO-ANGIITIS

Gangrene occurring in the relatively young—the presenile type—presents a different picture from that just described. It may have a variety of onsets, with intermittent claudication and symptoms referable to the deep vessels, with the appearance first of trophic changes, and an onset overlooked until the other extremity is affected. This disease is not confined to the Hebrew. One of the most striking changes in thrombo-angiitis obliterans is the extensive collateral circulation which may develop. While some collateral circulation may develop in arteriosclerosis it is not marked. Meleney and Miller in 1925 injected the vessels of legs of Chinese which had been amputated because of gangrene associated with a vascular change in every way similar to thrombo-angiitis observed in this country. Reichert had done this two years before, but his results were not published until later. A roentgenogram of the injected vessels indicates the loss of the normal arrangement of the blood vessels, and in the main vessels patchy defects

suggesting almost complete obliteration of the lumen at some points. In stereoscopic plates, numerous arterioles may be seen which extend even to the line of gangrene.

Meleney and Miller recognized the importance of this collateral circulation, for they state that if the disease continues instead of subsiding or coming to a standstill, a contest develops between two forces: blockage of the vessels on one hand and collateral blood vessel development on the other. There is a limit to the speed with which the collateral



Fig. 6—Injected specimen of leg and foot removed for gangrene associated with Buerger's disease, showing the development of a rather extensive collateral circulation, the capillaries are not injected as the injection mass does not pass into them.

circulation can develop. At present one can only guess what it is that limits the speed of the disease process, but the outcome is determined by the relative speed of the two. After an equilibrium has been established following the first attack, if a second attack comes on or a dormant process becomes active again, the contest is renewed, the margin of safety is narrower, the potential capacity of a collateral circulation is less and gangrene is more likely to develop.

It seems probable that the site of the thrombus may determine or modify the clinical course of thrombo-angitis obliterans. A thrombus originating in the femoral artery and descending is less apt to cause gangrene than a thrombus occurring in the anterior or posterior tibial arteries and ascending to the popliteal artery.

The possibility of an extensive collateral circulation developing in such cases is indicated by the injection of vessels of amputated legs and also by the postmortem observations in cases occasionally seen in which extensive thrombosis has occurred without marked circulatory disturbances.

I will cite the following interesting case, as it indicates how extensive such a collateral circulation may be.

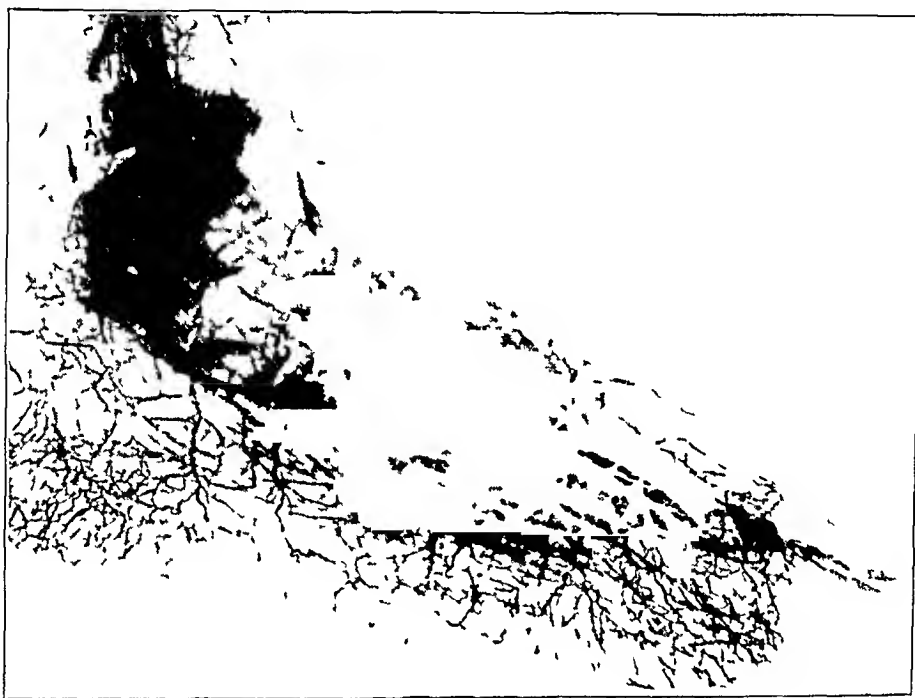


Fig 7—Injected specimen of foot in which amputation was done for thrombo-angitis obliterans, showing collateral circulation, at operation a recent thrombus was found in the popliteal artery.

REPORT OF CASE

W. W., a man, aged 47, of German extraction, was admitted to Johns Hopkins Hospital, Dec 12, 1926. About seven years before, while working at Quantico, Va., the patient noticed pains in the calves of both legs. These became worse and recurred more frequently until the summer of 1921. The condition progressed until he was unable to walk over half a block without the pain becoming so severe in both calves that he had to stop. About this time he noted that both legs would swell during the day. The swelling disappeared at night. One and one-half years later, similar pain and weakness developed in the right forearm when he worked. The pain would become so severe that he could not use his arm.

In July, 1924, an operation was performed for varicose veins. Multiple incisions were made on both sides, and sections of the veins were removed. The intermittent limping still persisted.

Physical examination revealed the man to be well developed and well nourished. The heart sounds were faint, a slight blowing systolic murmur being heard at the apex. The radial pulse was not palpable on the right side. The left radial pulse could hardly be felt, but the arteries were not like pipe stems. Scars of previous operations could be seen on the legs. Both feet were flushed. Pulses in the dorsalis pedis and posterior tibial arteries could not be felt, but the arteries did not seem to be sclerotic. When the legs were placed over the side of the bed the feet became bluish red and engorged. This discoloration persisted for several minutes when the lower extremities were placed on the level. The feet felt cold.



Fig. 8—Injected specimen of foot shown in figure 7, which demonstrates that the collateral vessels which are formed developed well up to the line of gangrene.

The hands were red, but blanched quickly when pressure was applied. Palpation of the brachial arteries failed to reveal any pulse on the right side; there was but a slight pulse on the left side. The carotid pulses were obtained with difficulty. Palpation of the femoral pulse was difficult because of the overlying fat.

Blood pressure readings could not be obtained in the right arm. On the left side the pressure was 136 systolic and 90 diastolic. It was suggested that the left femoral artery be tied. This was done. During the night the patient became hemiplegic and died.

I will quote at some length the pathologic observations, because they indicate how extensive arterial occlusion may be without marked functional disturbance.

The following paragraphs are taken from the autopsy record

The most interesting condition in the autopsy and that which appeared to be of the greatest significance was found in connection with the general arterial tree

At the level of the celiac axis the aorta suddenly became reduced in diameter so that it measured hardly more than 1 cm. There was an old organized thrombus which totally occluded the abdominal aorta beginning at the level of the celiac axis and extending all the way to the bifurcation. From about 5 to 8 cm below the celiac axis there was a small, crescent shaped channel which was the only



Fig 9—Histologic specimen of the left common iliac in cases cited in the text, showing multiple thromboses occurring apparently in a diffuse thrombo-angitis obliterans, the clinical history of the case would indicate that an extensive collateral circulation must have developed

channel which passed through this portion of the aorta. When a probe was passed through the channel from above downward it was found to end about 5 cm above the bifurcation, where it communicated directly with a comparatively large branch which left the aorta and spread out into the surrounding tissue. Below this branch there was no lumen within the aorta. It was totally blocked by an old organized thrombus which presented on section a peculiar transparent appearance. A complete blockage of the celiac axis had resulted from a comparatively fresh thrombus which extended from the celiac axis into the lumen

of the aorta or perhaps in the opposite direction. The portion of the thrombus which was in the lumen of the aorta communicated with the fresh thrombus which lay between the exit of the celiac axis and the organized thrombus which filled the abdominal portion of the aorta. The beginnings of the common iliac arteries were occluded by old organized thrombi which had many channels. The thrombosis affected the internal and external iliacs on both sides. The left external iliac, just before it became the femoral was only partially occluded by a thrombus. This was also true of the right external iliac. In the femoral artery on the left side extensive thrombotic changes were seen. None of the branches of the femoral group appeared normal.

In the right femoral region there were extensive thromboses of the femoral artery and its branches. All the main branches of the arch of the aorta showed sclerotic changes. Total occlusion of the second portion of the right subclavian was found, this extended into the axillary and brachial arteries. The right external carotid was closed by a thrombus. The point of origin from the common carotid was represented by a puckered scar. About 25 cm. above the bifurcation of the common carotid the internal carotid artery was found plugged by an organized thrombus through which passed small, newly developed channels. Proceeding upward into the skull a similar thrombotic process was found in the internal carotid at the point of anastomosis with the vessels from the opposite side.

This extensive process, going on apparently for years, must have been accompanied by an extensive collateral circulation, otherwise gangrene or death of tissues would have resulted.

I have quoted from this record merely to indicate how extensive thrombosis may be and still function be maintained by a collateral circulation.

There is definite evidence in cases of thrombo-angitis that gangrene in many cases is due to the extension of the process to the popliteal artery. Recent thrombi are not infrequently found in this vessel when an amputation is performed.

The indication in the treatment would seem to be to force the collateral circulation ahead of the advancing thrombus. Ligation of the femoral artery has been performed in seven cases, in four there has been a distinct improvement. In two cases ligation has been performed after gangrene had developed, subsequently amputation was necessary. In one case death followed the operation. Death resulted from hemiplegia thirty-six hours after the operation. In another case an infection was present and ligation was not attempted.

CONTROL OF PAIN

Pain in thrombo-angitis undoubtedly is due to a number of different factors. It may be a true arterial pain. In four cases the pain has been controlled. The operation puts at rest an inflamed artery. Its final result will depend on whether or not the collaterals which develop are diseased. An attempt is now being made to determine this.

That a collateral circulation does develop is also indicated by the frequency with which amputations through the middle of the leg are

successful in thrombo-angitis obliterans. The high percentage of failure in this type of amputation in arteriosclerotic gangrene indicates a difference.

In the treatment of so-called diabetic gangrene there must be the closest cooperation between the surgeon and the internist. Insulin has changed the outlook and has practically done away with that most distressing accompaniment of surgery, diabetic coma. Inflammatory processes increase the normal blood sugar. They produce the same effect, but to a great extent in the diabetic patient. Particularly in the case in which an infection has developed, cooperation should be the closest, for often it must be decided whether an operation should be performed in the presence of a marked hyperglycemia, because it is impossible to control it in the presence of infection, or whether it is best first to institute antidiabetic treatment with the hope of improving the patient's condition. Insulin has robbed diabetes of its distressing surgical complications. It cannot be expected to aid much in limiting the gangrene, for this is caused by the same mechanism as gangrene in the senile arteriosclerotic patient, the occlusion taking place at much the same level.

Either a transcondylar or a Gritti-Stokes amputation is the best.

In thrombo-angitis one is dealing with another process in which the development of a collateral circulation is a striking feature. One can attempt to keep the collateral circulation ahead of the advancing thrombus by ligating the femoral artery below the profunda, or, if amputation is necessary, the collateral circulation may be sufficient to permit an amputation through the leg. The development and behavior of the collateral circulation determines the line of procedure.

SUPRARENAL HEMORRHAGE

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AND

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REPORT OF A CASE

History—J C, aged 34, an Italian, married, salesman, entered the New York Hospital, First Surgical, or Cornell, Division, in the service of Dr Gibson Jan 25, 1925. His chief complaint was pain in the right side of the abdomen of two weeks' duration. Two weeks before entering the hospital he began to have dull pains in the abdomen in the epigastric region. They were not severe, and he continued to work until four days before admission to the hospital. At this time there was a sudden onset of sharp pain in the epigastrium, and he became faint. His bowels had not moved, and he took an enema. Soon after its introduction there was another sharp pain in the epigastrium, quickly shifting to the right hypochondrium. The pain was somewhat relieved by the enema but later became so severe that he called a physician, who gave him two hypodermic injections, which did not give relief. His condition steadily progressed and the pain was constant in the right side. He had some fever, but did not vomit at any time. The abdomen became distended but this condition was relieved by the enema. The past history was entirely negative, so far as he knew. He had always been an able-bodied, robust, hard-working man. The family history also was negative, to the best of his knowledge.

Physical Examination—This revealed a well nourished, well developed man slightly anemic and evidently acutely ill. Results of a thorough physical examination, including a neurologic examination, were negative, except for the abdominal observations and slightly inflamed tonsils. The man was of large build, bordering on the obese.

The abdomen was distended, tender and rigid. In the right lower quadrant and throughout the right side, there was a sensation of a mass lying in the right iliac fossa and extending upward in front of the kidney. It was approximately 15 cm in width, and perhaps 25 cm in length. It appeared 5 cm thick, and was retroperitoneal. The remainder of the abdomen was tympanic and slightly tender. Rectal examination revealed a tender mass in the right pelvis.

The urinalysis was negative for blood, pus and albumin. Examination of the blood showed 2,880,000 erythrocytes, with 35 per cent hemoglobin, 28,000 leukocytes, 86 per cent polymorphonuclear leukocytes and 14 per cent lymphocytes. His temperature on admission was 102 F, the pulse rate was 128, and the respiration was 32. The tentative diagnosis was appendicitis with abscess or possibly a perinephritic abscess. Neither diagnosis was completely satisfactory and an exploratory operation was decided on.

Operation and Course—A right rectus incision was made under nitrous oxide ether sequence, and the peritoneum was opened. A moderate amount of blood-stained serum with a few clots was found free in the peritoneum. A large mass of omentum appeared in the wound, and was pushed aside with pads. The entire ascending colon and the right half of the transverse colon and mesocolon were found to be the site of an enormous massive hemorrhage with old

and recent clots and some active bleeding when the mesocolon was split. The appearance was not unlike that of an extensive old necrotic hypernephroma. The right kidney was readily located, lifted from its bed and shelled out of its fatty capsule. Both seemed normal except for the extensive hemorrhage present everywhere. The kidney was replaced. Further exploration showed the hemorrhagic mass extending all along the vena cava inferior to the diaphragm, and downward into the true pelvis. A transverse incision through the right rectus outward to the quadratus lumborum gave excellent exposure, and a rapid but rather careful examination of all the abdominal organs did not reveal anything abnormal. Close attention was paid to the liver, spleen, gallbladder, stomach, duodenum, colon and appendix. The colon was freed by incising the peritoneum along the outer border, and large masses of clots were removed. Huge clots were present everywhere, in places well organized and apparently several days old. There seemed to be active bleeding, but arteries actually spurting could not be seen. The wound was packed firmly with two large Gibson Mikulicz tampons, and was partly closed with silkworm gut figure-of-eight sutures. The operation required thirty-five minutes.

The patient's condition became steadily worse during the operation. Two hours later, a hypodermoclysis of 1,000 cc was given. He received three hypodermic injections of morphine, one-fourth grain (0.16 Gm) each, also caffeine sodium benzoate, hypodermically. At 8 o'clock the next morning his temperature had risen to 103 F, his pulse rate had fallen to 120, and his respirations were up to 56. He died rather suddenly at 8 20 o'clock without any special symptoms.

The house surgeon's discharge note mentions an indefinite history of three weeks with pains in the arms and legs. He was uncomfortable, but kept at work until four days previous to admission. He then felt a sensation of mass in the epigastrium and moderate pain. After the enema there was a sensation of something giving way suddenly in the epigastrium and a shifting of the pain to the right side, with a feeling of weakness. After this another enema gave relief, but the pain persisted in the right side, and two days before admission it became so severe that he had to have hypodermic injections. He never vomited and never felt nauseated. He was markedly distended with gas. On admission he complained of pain in the right side of the abdomen with a palpable, tender, firm mass occupying almost the entire right half.

At operation the abdomen was found filled with free old blood, and there was a large old retroperitoneal blood clot. A hypernephroma was suspected but the right kidney was explored and found normal. The source of bleeding was not found. The condition became unfavorable on the operating table. Saline infusion and hypodermoclysis restored good quality to the pulse. This lasted until 6 o'clock the next morning, when there was a sudden change for the worse. He died at 8 20 a m.

Autopsy—Autopsy was performed by Dr Semsroth, at 1 30 p m. The diagnosis was adhesive bilateral pleurisy, fat infiltration of the liver, hemorrhage of the head of the pancreas, haemoperitoneum, extravasation of blood in the retroperitoneal space, chronic splenitis, old infarct(?) of the left kidney, chronic bilateral nephritis and suprarenal apoplexy on the base of infection.

The body was that of a well developed and well nourished white man. The skin was extremely pale, the hair black and normal in distribution. On the right side of the abdomen was a "T"-shaped surgical incision about 12 or 15 cm in length. The lateral angle of the horizontal incision was not closed,

and several rubber drains had been introduced through this opening into the retrocecal space. The surgical incision was opened and prolonged upward to the upper edge of the manubrium sterni. The retroperitoneal surface of the colon ascendens was covered with a rather firm blood clot measuring about 10 cm in length. The peritoneal cavity contained a considerable amount of free blood. Both pleural cavities showed a good many old fibrous adhesions between both leaves of the pleura, most pronounced at the bases diaphragmatica of both lungs.

The right lung weighed 500 Gm, the left 300 Gm. Both organs were crepitant throughout and failed to show gross lesions.

The heart weighed 500 Gm. The myocardium was fairly pale brownish red but did not show focal lesions. The edge of the mitral valve showed a few old thickenings. All other valves were intact. The ascending arch of the aorta showed a moderate amount of arteriosclerotic change. There were a few yellowish spots on the endocardium of the left ventricle near the aortic valve. The mitral valve measured 10 cm, the aortic valve, 6 cm, the tricuspid 11 cm, and the pulmonary valve, 8 cm. The thoracic aorta showed a slight amount of arteriosclerotic change.

The spleen was enlarged and weighed 300 Gm. The surface was grayish blue, but the cut surface was brownish red. The normal markings were rather cloudy. The pulp scraped easily.

The gastro-intestinal tract did not show gross lesions.

Part of the body of the pancreas was pushed aside by a cavity filled with a blood clot measuring about 5 cm in diameter. This cavity showed a free opening into the bursa omentalis. The bursa omentalis contained a large blood clot about 8 cm in diameter. The blood clot was separated from the tissue of the pancreas by a rather hard yellowish-white wall. Owing to the fact that most of the surrounding tissue showed an extreme bloody imbibition, a connection of the cavity with an adjacent artery was not found. Arising from this blood cavity a long mass of firm blood clot extended down into the retroperitoneal tissue, on the left side of the spine. The inferior vena cava was intact. The mesentery showed a considerable extravasation of blood near its root. The larger part of the pancreas, especially the tail, failed to show gross lesions.

The liver weighed 2,050 Gm, was about normal in size and showed a good deal of fat infiltration. The gallbladder was normal in appearance.

The right kidney weighed 150 Gm, the left 150 Gm. Both were enlarged. The capsule stripped easily. Section showed a patchy appearance, in parts grayish red, in other parts yellowish gray. The left kidney showed on one side large irregular thickenings. Section of this part showed that the cortex was narrow and cloudy. The pelvis and ureters failed to show gross lesions. The bladder and internal genitalia appeared normal. The abdominal aorta contained a postmortem blood clot. There was only a slight amount of arteriosclerotic change. The lymph nodes did not show gross lesions.

The suprarenals were not found. A specimen of abdominal viscera was fixed, to be examined carefully later.

The pancreas with the surrounding structures, was fixed in formalin. On cross-section of the blood clot near the inferior vena cava the suprarenal cortex was found embedded in the clot. The cortex did not form a closed ring around the medulla but the space normally occupied by the latter opened widely into the surrounding blood masses. The medulla could not be recognized but was replaced by a hemorrhage which showed a widely open direct connection

with the large retroperitoneal extravasations of blood. The suprarenal cortex itself was yellowish-white, and contained some brownish strands arising from the reticular layer. The portion of the splenic artery running on top of the pancreatic body was found intact, so that the first tentative diagnosis of ruptured splenic artery had to be rejected.

There was apoplexy of the right suprarenal medulla.

Microscopic Examination—There was a considerable amount of engorgement of the vessels of the lungs. The interalveolar capillaries at many places were



Suprarenal hemorrhage, showing extravasation of blood and diffuse infiltration with polymorphonuclear leukocytes, more dense at the borderline between the cortex and the medulla.

tortuous, protruding into the alveolar lumen. Many alveoli contained accumulations of desquamated epithelial cells. These desquamated cells contained a great many brownish-black minute granules varying in size and shape. These granules were likely to be blood pigment hemosiderin and were characteristic for high intrapulmonary blood pressure. The accumulations of cells loaded with pigment were most numerous near the pleural surface. At several places these cells were within the interstitial connective tissue and at some places also in the bronchial lumina. The interstitial connective tissue showed some accu-

mulations of mononuclear round cells, especially around some bronchi. There was moderate anthracosis. The pleura was thickened and showed some fibrinous coverings.

The muscular fibers of the myocardium at many places showed accumulations of yellowish brown pigment granules. These accumulations were spindle-shaped and were situated around the nucleus, the typical appearance and site of lipofuchsin granules. In the interfibrillar connective tissue especially around some vessels, were small accumulations of large cells. These cells did not show any regular arrangement. Some of them had a large, faintly stained nucleus, and some resembled lymphocytes.

The capillary vessels of the central parts of the lobules of the liver were engorged and dilated, the columns of liver cells appeared to be narrow. The cells of these parts often contained accumulations of small yellowish-brown pigment granules. On the other hand, the parenchyma cells of the peripheral parts of the lobules were swollen. They showed a cloudy granular appearance and the borderline of the cells were often indistinct. The periportal connective tissue showed a moderate round cell infiltration.

Passive hyperemia was present.

The number of pulp cells in the spleen was increased, and there was a moderate hyperemia. The number of trabeculae also appeared to be increased.

The renal epithelium showed an advanced parenchymatous degeneration. Some tubules contained hyaline casts, the intercapsular space of Bowman's capsule contained often mostly roundish red-stained homogeneous masses. The area showing in the gross thickening of the surface consisted of a uniform looking tissue. Here there was a considerable increase of the interstitial connective tissue. Scattered through this were many narrow tubules. These tubules were lined by a dense epithelium consisting of fairly small cells with large deeply-stained nuclei and bluish stained protoplasm. These cells had at many places lost their connection, and many of them were desquamated. They differed distinctly from those of the parenchyma by their smaller size, the bluish staining of the protoplasm and their dense arrangement. The glomeruli of these parts appeared intact, the interstitial tissue showed a diffuse cell infiltration. This area showed a sharp border against the parts just described. The medulla showed a considerable increase of interstitial connective tissue. At several places the area of a medullary ray was occupied by the same kind of lesion as that described, with numerous narrow tubules lined by a dense bluish stained epithelium. The vessels of these appeared engorged.

At many places the cortical epithelium of the suprarenal had a spongy appearance. In some parts there were extravasations of blood and diffuse infiltration with polymorphonuclear leukocytes especially in the reticular layer. At the borderline between the cortex and the medulla there were dense accumulations of polymorphonuclear leukocytes. The medulla was destroyed and was replaced by extravasated blood. The latter showed at several places distinct lamination, narrow strands of fibrin were at both sides covered with dense accumulations of leukocytes. These strands were situated between large accumulations of erythrocytes, so that the appearance of a thrombus resulted. At a few places the medulla appeared intact.

The diagnosis was suprarenal apoplexy on the base of infection.

REVIEW OF THE LITERATURE

Hemorrhages into the suprarenal gland are not uncommon. Indeed, if one includes cases of marked congestion of the suprarenal with any hemorrhages in the medulla, the condition is extremely common. Small

focal necroses are also found fairly frequently True abscesses are not so common, but have been mentioned in the literature

The first mention of suprarenal hemorrhage was by Moissenet and Rayer, and again by Rayer in 1837 This was followed by Valleix in 1838 The condition was not mentioned again until Matter's report in 1863, and that of Guemot in 1865 Hervey and Ahlfeld each reported cases in 1870

In 1902 Simmonds described suprarenal hemorrhage at great length He stated that the condition was common in the cortex, and that it usually followed acute infectious diseases, such as diphtheria, pneumonia, typhoid, osteomyelitis and sepsis It is probably toxic, as great amounts of bacteria are not found in the lesions Gross bleeding is rare, but infarction, hematoma and blood cysts are occasionally seen Symptoms may not be present, and yet the outcome may be fatal In some cases there are convulsions and signs of peritonitis Cases giving the picture of Addison's disease in the terminal stage have been described Simmonds had seen only one death caused by actual hemorrhage The patient was a man, aged 57, with sudden epigastric pain radiating to the back, followed by vomiting The diagnosis of peritonitis was entertained He died two days later Autopsy showed recent bronchial pneumonia and hemorrhagic infiltration of both suprarenals Thrombi were found in the veins of both, but inflammatory signs and micro-organisms were not present

Simmonds considers that many extensive bilateral hemorrhages should be regarded as antemortem and without symptoms or significance He reports a second case in a man, aged 53, with varicose ulcers and chronic heart disease, complicated by nephritis and embolism of the superior mesenteric artery He found hemorrhagic infarcts of both suprarenals, probably secondary and not the cause of the peritoneal symptoms He states that unilateral hemorrhage may cause large tumors with grave symptoms, and that occasionally surgical intervention is necessary Few cases have been noted in the literature He quotes Pawlik, who reported the death of a woman 40 years of age The abdominal cavity contained 10 liters of old blood clots He mentions a case of Chiai, who reported a blood tumor which weighed 6 kilograms There was no neoplasm, but there were bleeding and calcareous concretions in one suprarenal

Simmonds considers the etiology as variable Trauma is the cause in certain cases and even the destruction of the suprarenal vessel may follow contusion (Wallman) Hemorrhage in the suprarenal of the new-born is common If the child lives, the hemorrhage is resorbed It is seldom seen in later infancy He has never seen large hematoma of the new-born He quotes Ahlfeld, who had a patient who presented a bilateral hematoma the size of a hen's egg Another case is described

CONCLUSIONS

Hemorrhage into the suprarenal is a fairly common condition. It is possible that some hemorrhages of minute quantity are not abnormal. Probably many occur shortly antemortem, and are not of significance in themselves.

Suprarenal hemorrhages may be unilateral or bilateral, of large or small size, confined to the capsule or spreading into the retroperitoneal tissue, or even into the peritoneal cavity. Spontaneous recovery undoubtedly occurs. Diagnosis of this condition is extremely difficult, and it is doubtful whether it can ever be definitely made antemortem.

Massive hemorrhages which result in large collections of blood may at times be palpated, and they are suitable for surgical procedure, if the diagnosis can be established.

1. The first part of the paper
describes the general principles
of the method.

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The second part of the paper
describes the details of the
method. It is divided into
three sections. The first
section describes the
general principles of the
method. The second section
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describes the results of the
method.

6.

vidually or together. In the cases of the series reported in the previous communications, the jaundice was usually mild and temporary, and the nephritis was symptomless and for the most part a "laboratory" phenomenon. In the milder forms of biliary tract disease no differences could be noted, as far as the nitrogen bodies of the blood were concerned, between the uncomplicated cases and those in which these milder forms of jaundice and of nephritis were present.

In a considerable percentage of the cases, changes in the nitrogen bodies of the blood were demonstrable after operative intervention. In a general way, the relationship of the ante-operative to the postoperative observations could be classified in the following three groups:

1 A group in which the preoperative and postoperative status was practically identical.

2 A group in which the postoperative status showed a regression from the preoperative status.

3 A group in which the postoperative figures showed a progression from the preoperative status.

All that one is permitted to say in regard to the cases in the first group—with comparatively identical preoperative and postoperative figures—is that the net result of whatever has happened *pari passu* with the operation and during the convalescence, as a consequence of any factor associated with either the original disease or the operation, has been insufficient to disturb the status existing before operation. Such cases are not necessarily restricted to the group in which the operation is not followed by any complication, *i. e.*, jaundice or nephritis, or both. To a smaller extent, cases were observed in which jaundice or nephritis appeared after operation, and under such conditions it seemed fair to assume, not that changes did not occur, but that their perceptible effects were rectified by the compensatory mechanisms.

The cases in the second group—those with postoperative regression from the preoperative status—are extremely interesting. From preoperative observations alone, it had been assumed prior to operation that the figures obtained were "normal." In the light of the consistent diminution in the figures that occurred in this group after operation, it seemed more correct to say that the preoperative status is "abnormal," and that the postoperative change indicates an improvement in the condition. This illustrates the importance of not making judgments based on any individual observation—a fact to which we have referred several times. The regressive changes of the second group were observed most often in cases of long standing and in uncomplicated cases as well as in cases associated with nephritis or jaundice.

function follow quickly and to an equal extent and may ultimately become of extreme grade, even progressing to a terminal toxemia. The ultimate stage of such liver shrinkage is found in acute yellow atrophy of the liver. Leucin and tyrosin are then frequently found in the urine.

2 A sudden and large diminution in the discharge of bile from an external biliary fistula after operative relief of an obstruction and in the absence of any further obstruction when the amounts of bile simultaneously discharged into the intestinal tract remain constant as evidenced by stool examination. This never occurs unless there is marked interference with the normal activities of the hepatic cells, and it indicates a state of functional incompetence second only to that seen with the milder grades of acute yellow atrophy. The origin of the jaundice that usually accompanies this phenomenon is intimately associated with the diminution of the excretion of bile, it is found in the hepatic cell. According to the work of Eppinger and others, the mechanism of the jaundice is an interference within the confines of the cell with the passage of bile components into the bile capillaries. Toxemia of various grades is present.

3 An external biliary fistula from which large quantities of bile escape from the organism for shorter periods of time or smaller quantities escape over long periods of time. Continued or extreme bile wastage leads to other subjective and objective symptoms which are presently to be noted.

4 Obstruction of the common duct. This operates through the profound jaundice which it causes.

5 Deepening or very deep grades of jaundice in the presence of an open common duct or in the presence of a discharging external biliary fistula, especially when the quantity of bile discharged remains constant.

Severe grades of jaundice or deepening jaundice is an important indication of severe lesions and follows and coexists with or is shortly followed by, changes in the liver cells which lead to undermining physiologic disturbances. Quantitative estimations of the bilirubin content of the blood serum (van den Bergh) are roughly proportionate to the depth of the existing jaundice and are extremely valuable for this purpose in clinical practice. These estimations were constantly employed in these studies.

Many of the items listed in this classification as phenomena associated with a severe type of biliary tract lesion result directly from the presence of jaundice. This includes both subjective and objective phenomena. The most important of these are

1 Hemorrhage

2 The presence of renal complications as shown by the laboratory evidences of nephritis (or nephrosis) and by a diminution of the fluid output.

3 The development of acidosis or of an alkalosis

Combined subjective and objective phenomena occur. These include

1 Loss of vasomotor function—flagging in the strength of the cardiac function and in the quality and fulness of the pulse.

2 Loss of weight and strength. This is an important item and is due to other factors, such as insufficiency in food and fluid intake, to the loss of bile and to vomiting.

3 Deterioration in the general condition of the patient, lassitude and inaptitude for any exertion—sluggishness of movement, and other symptoms. These, too, parallel other factors and are dependent on them, especially on bile wastage, and form valuable criteria for making judgments.

4 The development of a peculiar form of toxemia ("cholemia") in which sluggishness of the vital faculties and various grades of coma form the most important parts. This always indicates the most severe grade of disease, and usually indicates an approaching fatality. Commonly the toxemia is associated with deep grades of jaundice.

As the severe types of cases under discussion come under observation they are found to fall into two broad groups: the group in which operation was not performed and the group in which operation on the biliary tract had previously been performed.

OPERATION NOT PERFORMED

The group in which operation was not performed contains cases in which the total duration of the symptoms is only a matter of weeks or months, in these it is noted, however, that the progression of the biologic development has been rapid. The symptomatology includes the usual biliary colic and attacks of cholecystitis, fever, possibly chills, initial or later vomiting, loss of weight and strength and at least some of the phenomena included in the preceding classification. Jaundice is almost always present, it usually deepens under observation, is always of severe grade, is frequently accompanied by secondary symptoms, especially hemorrhage, can be followed clinically by the variations of the van den Bergh test and quickly assumes a dominant position in the clinical picture. Renal complications—nephritis, nephrosis (renal epithelium degeneration)—may not be demonstrable. When present, the latter frequently begin as laboratory phenomena, and as such, possibly play no part in the clinical picture, later they can, and do, assume proportions of their own. When there is persistent vomiting there is a consequent diminution in the food and fluid intake which is quickly reflected in a similar or exaggerated diminution of the fluid output, the latter, however, may also be the only indication of renal damage.

All grades of severity are seen in clinical practice. In the most severe cases, there are laboratory evidences of an increasing acidosis, finally, a toxemia develops associated with coma, with the deepest forms of jaundice, carphologia, loss of control of the sphincters, Cheyne-Stokes breathing and other symptoms. The cases in which the latter phenomena occur are invariably fatal.

In other cases in which operation has not been performed and in which the disease has existed for a number of years, the individual manifestations—i. e., the attacks of cholecystitis—are separated by variable and fairly long intervals of apparently good health. Finally an attack

occurs in which the manifestations are more marked than the previous ones and in which they assume the characteristics of those described in the preceding paragraphs

The group in which operation has not been performed also contains cases in which the progression of the illness and its symptomatology is a fairly continuous one. At a certain stage of the development, the symptom complex assumes a severity out of all proportion to the previously existing manifestations, and it becomes similar to that described in the preceding paragraphs

In the cases in which operation is not performed the transition from a mild or moderately severe form of biliary tract disease to the severe form considered in this discussion is commonly associated with a well defined factor which is easily recognizable in the clinical picture. This change is commonly associated with a more or less complete obstruction of the common bile duct. Case 99 forms a good illustration of this type, and includes illustrative features common to all cases in the group in which operation is not performed

CASE 99—A woman, aged 60, had been having attacks of right hypochondriac pain with fever, vomiting and jaundice at irregular intervals for the preceding five or six years. The present attack resembled the previous ones, except that the general symptoms seemed more severe, the jaundice kept increasing in intensity, the general condition of the patient was becoming increasingly poor and stupor was developing

The physical examination confirmed these facts. Obstruction of the common duct was absolute, the jaundice was most intense and grew deeper under observation, the patient was stuporous and on the verge of deep coma, and the condition of the circulation and of the general well-being showed marked decomposition and deterioration. Except for some distention, the abdomen yielded no positively abnormal facts. The rest of the physical examination disclosed nothing abnormal. There were laboratory evidences of an acidosis (diacetic acid in the urine) without glycosuria or hyperglycemia. The urine showed the presence of an acute nephritis (albumin, casts and other elements), the phenolphthalein excretion was 10 per cent in the first two hours, nevertheless, the kidney output (1,100 cc) was sufficient. There was no nitrogen retention (urea nitrogen, 17, nonprotein nitrogen, 28, uric acid, 1, creatinine, 1, cholesterol, 0.32 and carbon dioxide, 48 per cent) in the blood

The patient received a transfusion with 500 cc of blood, and large quantities of glucose were given intravenously in a 5 per cent solution. Under these therapeutic measures, there was a remarkable temporary improvement which lasted about twenty-four hours. Then the stupor and coma reappeared and deepened, and the same therapeutic measures were repeated. The improvement thereafter was not nearly so marked. On the morning of the second day, the general condition of the patient was bad, the condition of the cardio-respiratory system was poor, there was deep coma, Cheyne-Stokes respiration and other signs of a profound toxemia. The patient died soon afterward with the typical picture of a "cholemia"

Postmortem examination of the body showed an extensive cholelithiasis occupying the common and major portions of the hepatic ducts, an acute cholangitis, multiple abscesses in the parenchyma of the liver and an acute renal swelling and degeneration of the renal epithelium

This case illustrates (1) the occurrence of a severe biliary tract lesion in a patient not operated on, (2) the general symptomatology, (3) the presence of subjective and objective symptoms and the laboratory data on which the gravity of the disease is measured, (4) the presence of the determining factor, obstructive jaundice, with which infection is associated in this particular instance, (5) the temporary relief of symptoms after free mobilization of glucose, (6) the occurrence of a secondary renal degeneration, and (7) the terminal toxemia (cholemia), which because of facts to be presently discussed in this communication, especially the absence of blood nitrogen retention must be assigned for the major part to an hepatic origin and to a much less extent to the renal factor

In rare instances the transition to the severe type of case is associated with a severe form of infection which almost always assumes the clinical manifestations of an acute yellow atrophy of the liver. Case 100 illustrates this type of case

CASE 100—A married woman, who had borne two healthy children and who had previously been free from any attack similar to the present one, was seized two weeks before admission to the hospital with sharp epigastric pain which radiated to the right side of the back and to the scapula, vomiting occurred and fever developed. Three days after the onset, she became jaundiced, the pain and jaundice continued, the urine darkened progressively, and the stools became clay colored. At the beginning of the condition the physician was able to feel a much swollen liver which extended several fingerbreadths below the costal margin, but in the days following, the size of the liver lessened appreciably every day.

On the day of admission to the hospital physical examination showed (1) a patient who was well nourished and appeared acutely ill (2) a general tendency to inactivity, (3) sluggish reactions of the various faculties to stimuli, (4) an intense jaundice of the skin and of all of the mucous membranes and (5) a liver which was palpable below the costal margin and which had a sharp edge and a smooth and not tender surface. The rest of the physical examination gave no positive abnormal conditions.

Late in the day of admission, the patient suddenly became stuporous. During these few hours, the jaundice increased in intensity, a stool which was evacuated was clay colored, and the liver receded under the costal arch so that it was no longer palpable. There were distinct signs of liver insufficiency, the patient vomited profusely, she was restless and irrational and there were marked twitchings of the face and extremities.

On the next day, the patient was much worse. She was in deep coma. The jaundice was apparently still increasing and she had lost all sphincter control. The vomitus consisted of chocolate-like material. The edge of the liver was not palpable and its outline was obscured by tympany. Irritative phenomena

occurred, referable to the central nervous system. A uremic odor to the breath was perceptible. Finally there was Cheyne-Stokes breathing. The patient died shortly afterward.

During the short stay in the hospital there seemed to be some restriction in the output of urine, examination of the later showed a heavy trace of albumin, much bile and an occasional white cell in the microscopic field. The Wassermann reaction was negative. The nitrogen status in the blood was as follows: urea nitrogen, 15.4, nonprotein nitrogen, 35, uric acid, 13, and creatinine, 1. The blood contained 0.086 gm of cholesterol per hundred cubic centimeters, and the carbon dioxide content was 40.

The postmortem examination of the body showed (1) a gallbladder with much thickened walls containing about twenty-five stones lying in a thick, light green, turbid bile, which had a purulent odor, (2) empty cystic and common ducts, (3) thickened and edematous walls of the common duct and a lumen containing bile similar to that in the gallbladder, (4) a normal hepatic artery, (5) negative portal and hepatic veins, (6) a typical acute yellow atrophy of the parenchyma of the liver, (7) several enlarged hyperplastic lymph nodes along the duct, (8) a swollen, congested spleen with enlarged lymph nodes at the hilum, (9) moderately enlarged retroperitoneal and mesenteric lymph nodes, (10) normal suprarenal glands and (11) enlarged, deeply congested kidneys from which the capsules stripped with ease.

We interpret this condition as a case of cholelithiasis in which an acute yellow atrophy of the liver was the terminal phenomenon of an extremely severe infection of the biliary tract. The case is differentiated from the preceding one by the character of the determining factor (infection as opposed to obstruction) and by the lack of recuperative power in the presence of this terminal lesion. It resembles the first case in the remainder of the manifestations. The presence of a low uric acid content in the blood is remarkable. This clinical fact is not in conformity with the observations of Mann and his co-workers who, in experimental work, found high uric acid contents in the blood after removal of the liver.

OPERATION PERFORMED

In the group of cases in which operation has been performed the symptomatology of the severe type of case under discussion parallels closely that given for the cases in which operation was not performed, and the differences, if any, incline themselves to an increase in severity of the individual manifestations or of the total symptom complex regarded as a whole. Many or all of the phenomena classified previously as indicating the severe type of biliary tract disease are constantly present, the patients are extremely sick, and severe forms of toxemia are frequently present.

The group of cases in which operation was performed contains instances in which the transition to the severe type occurs in such close proximity to an operation as to compel the belief that there is a causal relation between some factor associated with the operation and the

appearance of the severe symptoms. One cannot escape the impression that in many cases the anesthetic employed is the most likely factor. The simplicity or severity of the operation which has been performed seems of little importance. Case 96 seems to fall in this group.

CASE 96—A simple cholecystectomy was performed on a woman for an inflamed gallbladder. The interior of the gallbladder contained a calcareous deposit, and there was numerous pericholecystitic adhesions. A perforation was present in the wall of the gallbladder, and it reached into the parenchyma of the liver. Jaundice was not present before operation, and the kidneys were clinically "normal."

TABLE 1—Laboratory Data for Case 96

Date	In take, Cc	Out-put, Cc	Urine					Blood						
			Albu min	Casts	Bile	Total Nitro-gen, Gm	Van den Bergh Estima-tions	Urea Nitro-gen	Non protein Nitro-gen	Uric Acid	Creat inine	Choles terol	Carbon Dioxide, Per-cent	Age
June 14														
15		630												
16		630												
17		960												
18	2 010	1,110												
19	3,320	1,440												
20	2,590	1 340												
21	1,890	1,440												
22	1,530	1,170												
23	1,800	1,110												
24	1,630	1,850												
25	2,010	1,260												
26	2,010	1,230												
27	2,100	1,770												
28	1,980	1,880			+									
29	2,220	1,560												
30	1,770	1,500			+									
July 1	2,100	1,050	Tr	0	+		1 7700							
2	2,400	1,500	Tr	0										
3	2 490	690+												
4	2 890	1,050+	+	0										
5	2,550	1,380+	++											
6	1,580	900+	+	0										
7	1,080	780+			++	6	1 25000	12 6	31 5	2 0	1 0	0 088	46 2	
8	1,680	1,350+	Tr		+									
9	2 880	1,200												
10	2,640	890+	Tr											
11	2,250	990+	0	+										
12	840	1,290												
13	2 820	1,500+	0	+										
14	1 680	720	0	0			1 110000	12 6	35 0	2 0	1 0	0 094	59 5	
15	1,200	?	0	0										
16	1,230	1,080+												
17	1 740	?												
28								14 0	34 1	2 5	1 0			

Four days after operation, the patient became jaundiced, the condition increased in intensity during the succeeding days, and the stools became acholic. The patient vomited whatever she ingested, and the symptom grew worse concomitantly with the increase in the jaundice. At the end of about ten days, the patient was distinctly stuporous, and the various faculties were distinctly apathetic. Coincident with the appearance and progression of these symptoms, the discharge of bile, which previously had been moderate, became markedly restricted in quantity and consisted of a thick, yellowish, mucoid, extremely turbid fluid.

The main reliance in treatment was placed on (1) transfusions of blood (2) infusions of 5 per cent dextrose solutions, intravenously, and (3) the administra-

tion of abundant supplies of fluids of all kinds. The symptoms gradually improved, the jaundice lessened, and the vomiting finally stopped, the progressive improvement became permanent, and the patient recovered. At the time of discharge, jaundice was still present but steadily lessening. The laboratory data are given in table 1.

The group of cases in which operation was performed contains instances in which, following operation for the relief of obstruction of the biliary tract (common duct), the previously existing symptoms either do not become ameliorated or become aggravated. The presence of the biliary obstruction makes this a severe case from the beginning and the lack of improvement after operation and adequate drainage of the common duct is probably related to an advanced pathologic process or an advanced pathologic physiology, or to both of these factors together. The aggravation of the manifestations is undoubtedly often increased by the effects of the anesthetic drug on the renal, and to a lesser degree on the hepatic, parenchyma. A low grade of toxemia is commonly present, with nausea, vomiting, diminution of fluid intake and output and with loss of weight. Fulminant forms of toxemia also occur and a fatal issue follows rapidly. Cases 91 and 104 illustrate this type of case.

CASE 91—A man, aged 73, had a persistent jaundice preceded and accompanied by pain in the right upper quadrant of the abdomen, with periods of remission in the intensity of the jaundice. Physical examination revealed a slightly enlarged liver and a moderate degree of emaciation, and confirmed the presence of the severe jaundice. A test of the function of the liver showed 30 per cent retention at the end of one hour. The phthalein test averaged between 80 and 90 per cent excretion at the end of two hours. A single obstructing stone found in the common duct at operation was removed, a cholecystectomy was done. In spite of the fact that the wound in the duct was sutured, drainage of bile occurred immediately and was profuse. Convalescence proceeded in the customary manner for the first two weeks. There was some diminution in the jaundice at first, but later it increased, and continued to be severe throughout the duration of the illness. On the seventeenth day after operation, the patient began to hiccough and vomit. The appetite grew poorer. The general condition continued to deteriorate in spite of all measures employed, and the patient died at the end of a month. Postmortem examination was not performed. The laboratory data are given in table 2.

CASE 104—A woman, aged 60, had had numerous attacks of right hypochondriac pain. Several days before admission she had a severe attack of acute cholecystitis, and she became jaundiced. At operation, an acutely inflamed gallbladder was found, and stones were present in the gallbladder and in the common duct. Following operation, the temperature rose rapidly, and the patient developed marked toxemia which seemed clinically to be typically "cholemic." Death occurred one day later. There was no time or opportunity to make laboratory studies, and postmortem examination was not performed.

The group of cases in which operation was performed contains instances in which a simple operation had been performed at an appreci-

able interval before the present moment of observation, the patients had gone through these primary operations—usually a cholecystectomy or cholecystostomy—with no extraordinary manifestations and recovery had been uneventful. Later, there was a recurrence of symptoms, these reproduced the previously existing symptom complex or presented new manifestations, in any case, the further development of the clinical picture followed along the lines already described in this communication,

TABLE 2—Laboratory Data for Case 91

Date	Intake Cc	Output, Cc	Liver Function Test, Percentage	Nephritis	Urine Bile	Phenolsulphonphthalein Test Percentage	Total Nitrogen Gm	Stool	Stool Urobilin Gm	Van den Bergh Estimations	Urea Nitrogen	Nonprotein Nitrogen	Urine Acid	Creatinine	Cholesterol	Carbon Dioxide Percentage
March 9			30	0	+	90				1 50000	18.2	31.5	3.5	1.2	0.260	48
12	480	890														
13	960	660														
14	1 020	1 030														
15	2,490	1 200		+		80				1 30000	28.0		2.5	1.3	0.170	
16	2 220	1,680														
17	1 980	1,020														
18	1 800	1,080														
19	2 160	1 200														
20	2,220	1 200														
21	1,050	1 520														
22	1,680	1,440														
23	1,200	1,080				76		Brown		1 50000						
24	1 500	1,200														
25	1 980	1 740														
26	2 240	1 500														
27	2,640	1 870														
28	2,640	1,040														
29	3 120	660														
30	3 750	1 140					15 66									
31	3,840	1,050														
April 1	720+	300														
2	2 130	360									22.4		2.5	1.2		
3	2 730	360														
4	3 420	480														
5	3 150	720							0.045							
6	2 640	750														
7	2 820	1 440		++							22.4	52.5	2.5	1.3	0.206	60
8	2,670	960														
9	2,700	480														
10	1,020	840														
11	600	480														

both in the unoperated and in the operated groups of cases. Some form of obstruction of the common duct is usually present in these cases. Commonly the obstruction is due to stones, less frequently to tumor especially a carcinoma of the pancreas or of the common duct at the papilla, more rarely to stricture of the common or hepatic ducts. Frequently the patient's condition continues at a relatively low status for a certain length of time until some particular factor causes a sudden change for the worse and finally death.

TABLE 3—Pathologic and Laboratory Data of All Cases in This Communication

Case No	Liver Lesion	Phenol sulphonic phthalic test	Ne Jaun dice	Urine Bilirubin	Van den Bergh Index	Urea Nitrogen	Non protein Nitrogen	Urine Creatinine	Phenol-sulphonic phthalic test	Ne Jaun dice	Urine Bilirubin	V in den Bergh Index	Urea Nitrogen	Non protein Nitrogen	Urine Creatinine	Urine Acid	Urine Great line	Result
74	Infiltration		0	0	0	12.6	30.9	1.3	1.1	0	0	0	15.4	35.0	2.0	1.0	Well	
75	Chronic cholangitis, fit infiltration, cholelith		+	+		21.0	60.0	2.2	1.1	+	+		21.0	40.0	2.3	1.5	Died	
75	Infiltration		0	0		18.2	36.7	2.6	1.1	+	+	1	40000	122.5	6.5	1.3	Well	
80	Cirrhosis		0	0	1 200000	15.4	34.1	2.5	1.0	0	0		18.2	35.5	2.5	1.0	Well	
83	Chronic pericholangitis		0	0	1 120000	22.4	51.2	3.9	2.0			1	400000	19.6	3.5	1.2	Well	
90	Fatty infiltration, passive congestion		0	+	1 5000	11.0	35.0	2.8	1.3	+	+		10.6	94.4	3.0	1.0	Died	
91	Cholangitis, degeneration		0	+	1 50000	18.2	31.5	3.5	1.2	+	+	1	30000	52.5	2.5	1.3	Died	
85	Necrosis, purulent cholangitis		0	0	1 75000	18.2	35.0	4.0	1.1				22.4	52.5	Immediate		Died	
71	Early cirrhosis		+	0		22.4	66.3	2.7	1.8								Well	
81	Acute suppurative cholecystitis	80%	0	0		29.4	57.7	3.3	1.0	+	+		29.4	61.0	3.0	1.0	Well	
82	Empyema, stones, obese and sick		0	0		29.4	57.7	3.3	1.0								Well	
98	Cholecystitis, postoperative vomiting		0	0	1 150000	26.6	50.0	2.5	1.0								Died	
97	Acute cholecystitis, exacerbation, slight postoperative acidosis	70%	0	+	1 200000					+	+		54.6	129.5	2.1	1.2	Well	
99	Duct obstruction by stones, jaundice cholangitis with multiple abscesses of the liver, abscesses in the lung, acute renal swelling and nephritis, acidosis, carbon dioxide, 18%	10%	+	+	1 5000	17.0	28.0	1.0	1.0	No operation			65.8	136.7	7.5	2.1	Well	
100	Chronic cholecystitis, acute yellow atrophy, renal congestion, cholelith		0	+		15.1	35.0	1.3	1.0	No operation							Died	
96	Chronic cholecystitis, pericholecystitis, pericholecystitis with perforation into liver, postoperative jaundice with cholelith		0	0						+	+	1	7700	31.5	2.0	1.0	Well	
94	Chronic cholecystitis, postoperative vomiting, nausea, etc., toxemia		+	0						15%	+	1	50000	109.2	11.0	2.0	Well	
80	Degeneration		+	0		29.4		5.3	2.0								Died	

LABORATORY OBSERVATIONS

Table 3 contains all of the available pathologic and laboratory data of the cases studied for this communication. The cases were selected only for the severity of their clinical and other manifestations, but were otherwise taken seriatim as the patients were consecutively admitted and discharged from the hospital. In all of the studies, special attention was paid to the surgical problems involved as they were related to the study of the blood chemistry.

A summary of the deductions to be made from this table include the following:

1. The severe type of biliary tract disease is almost invariably associated with definite changes in the parenchyma of the liver.

2. The severe type of biliary tract disease is more commonly associated with jaundice and with renal changes than the mild or moderately severe type of case.

3. The preoperative nitrogen body content of the blood does not differ markedly from that in mild and moderately severe cases of biliary tract disease. This seems to hold good, at least as far as the cases studied in this communication are concerned, both for the blood figures as a whole and for the individual groups.

4. The postoperative nitrogen body content of the blood shows, consistently, increases over the preoperative status, these follow along the line outlined in the preceding papers. A decrease occurs after operation in only one instance in the cases in the table. In at least one-third of the cases these increases are extremely large.

5. When large postoperative increases of the nitrogen body contents of the blood occur after operation, the blood figures have been reliable indications of the gravity of the entire clinical picture, subsequent regression to normal levels has accompanied amelioration of the pathologic condition, either temporary or permanent, their progression has indicated an equal progression of the illness.

6. The prognosis in the severe type of biliary tract disease is extremely grave, 41 per cent of the cases studied in this communication have terminated fatally.

The following cases illustrate the relationship of the various clinical and laboratory data on which a discussion of the problem is based.

Case 75 illustrates the relation of the fluid intake and output in this group of cases to the blood figures.

CASE 75.—A cholecystectomy was done after an acute exacerbation of a chronic cholecystitis, cholelithiasis was present also. Laboratory evidence of a moderate nephritis was present. During the acute attack, the patient became

jaundiced, and bile in moderate amounts was present in the urine. The laboratory data are given in table 4.

There was no apparent increase in the nephritis after the operation. No change was noted in the degree of jaundice. About ten days later, the patient's appetite began to flag, this condition increased and became associated with vomiting. A free discharge of bile occurred from the wound, and bile continued to pass into the intestinal tract. Acidosis developed later, which was probably due to the marked restriction in food and fluid intake. There was a tendency to diminution in the fluid output of the body. The symptoms continued, and the patient finally

TABLE 4—Laboratory Data for Case 75

Day of Illness	Clinical Notes	Nephritis	Acetone	Diacetic	Jaundice	Urine Bile	Van den Bergh Estimations	Fluid Intake Cc	Fluid Output, Cc	Urea Nitrogen	Non protein Nitrogen	Uric Acid	Creatinine
Ante operative		++			+	+				21.0	60.0	2.2	1.1
September 4, operation													
Postoperative Sept													
6		++				+		3,300	?	21.0	40.0	2.3	1.5
7								6,400	1,140+				
8	Pneumonia							3,000	1,200+				
9								1,080	?				
10		+						1,200+	1,140+	14.0	34.1	1.6	1.0
11								1,380	1,170				
12								2,340	1,500				
13								2,100	1,740				
14								2,040	1,620				
15	No bile drainage	+						2,160	1,740	14.0		1.6	1.0
16								2,100	2,220				
17								2,040	1,800				
18								1,440	1,380				
19	Profuse bile drainage							1,780	1,440				
20								1,380	1,380				
21								1,440	1,380				
22	Complete anorexia, nausea, vomiting free discharge of bile, bile in stool					+	170000	1200	?	18.2	34.2	2.7	1.2
23								720	600				
24	Symptoms continue as on September 22	+	+	+		+		540	600				
25								720	960				
26								360	1,140				
27								840	1,380				
28								600	1,140				
	Ceased												

died. The increase in fluid output during the last few days of life must be accepted as evidence that the excretory mechanism of the body was beginning to recuperate.

The postmortem examination of the body showed a marked fatty infiltration of the liver with marked fibrosis around the portal spaces, there was no acute inflammation. There were changes in the kidneys also.

CASE 94—The patient was first operated on in 1914 at the age of 36. At that time a large stone was found in the common duct, and much bile sand was present throughout the demonstrable portions of the biliary tract. A cholecystectomy was done and the ducts were drained, the patient recovered. In 1922, he began to have attacks of typical biliary colic with jaundice and clay colored

stools, nausea, chilliness and fever. In 1923, he was operated on again. Stones had again formed in the common duct, and the walls of the duct were enormously thick. The stones were removed, and drainage of bile from the common duct was instituted.

At the end of the first week after operation he began to vomit and his general condition began to deteriorate. Ten days after operation the drainage of bile had become scant. Signs of a nephritis developed. Five days later, signs of toxemia (uremia?) were marked. Under conservative forms of treatment (5 per cent dextrose infusions, blood transfusion, forcing of fluids generally) these symptoms gradually disappeared, and the patient finally recovered.

The postoperative laboratory data are given in the chart.

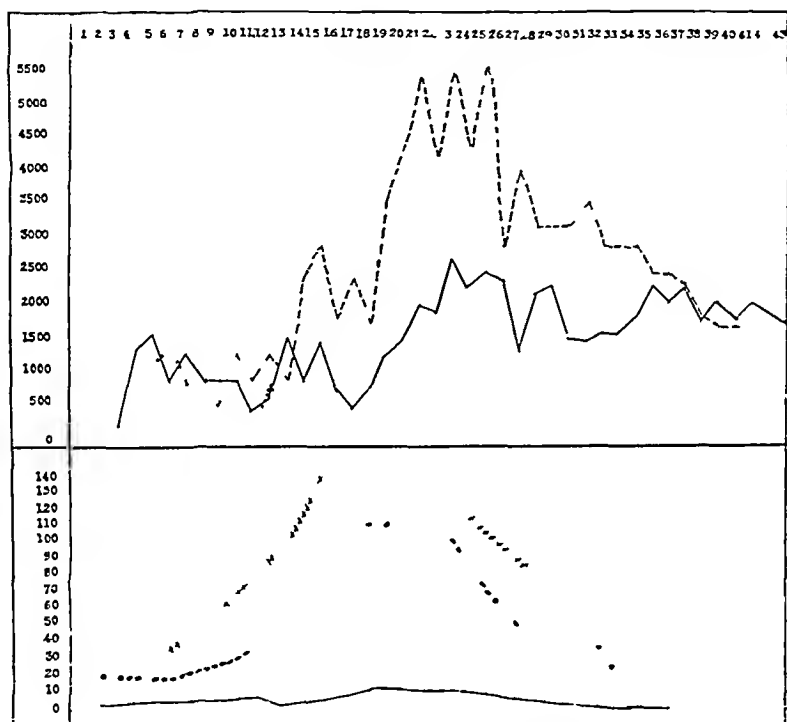


Fig 1—Laboratory data in case 94. In the upper part of the chart the broken line indicates the food and fluid intake, the unbroken line the fluid output, and the dotted line, the bile drainage. In the lower part of the chart, the dotted line indicates milligrams of urea nitrogen per hundred cubic centimeters, the crosses, the nonprotein nitrogen and the unbroken line, the uric acid.

CORRELATION OF CLINICAL AND LABORATORY FACTS

The segregation of the group of cases embodied in this communication has not been simple. Various difficulties have arisen, not the least of which has been the selection of the cases in which the progression of the disease has been sufficient to enable one to classify it as a severe case. Cases have occurred constantly which at first sight have appeared to be mild cases or moderately advanced cases and in which the later development of the clinical picture or the nature of the postoperative

phenomena have compelled the inclusion into the severe group. The opposite has happened also. As far as possible, only those cases are included in which we have been sure of our ground.

The chief reason for this difficulty lies in the enormous compensatory activity of the liver and its associated organs, especially the kidneys. Laboratory evidence is abundant in proving this point. Far advanced pathologic processes therefore may and do occur before an adequate symptomatology is presented to the clinician, this is true not only as far as subjective and objective symptoms and manifestations are concerned, but even more so of laboratory evidence. In all of the studies in this and in the previous communications, this factor has been extremely important and has interfered markedly with the proper valuation of the demonstrable evidence.

The outstanding facts in these studies are

- 1 The comparatively restricted field in which the results of biliary tract lesions have established effects when the duration of the disease has been short and the manifestations of the disease could be classified as "mild." In the early stages of lesions of the biliary tract, there have been few pathologic changes and, for practical purposes, no physiologic changes have occurred.

- 2 In the mild cases, the total absence of complicating factors, especially of jaundice and renal changes. These begin to establish themselves in the group of moderately advanced cases, and assume their greatest frequency as the cases present more and more of the severe manifestations.

- 3 The great frequency with which the severe manifestations are associated with obstructive jaundice.

- 4 The relative frequency with which the case has passed from a mild or moderately severe form to the severe form discussed in this communication directly after operative intervention.

- 5 Most, if not all, of the primary physiologic disturbances are due to secondary effects on the hepatic cell.

The first disturbances that have been perceptible have seemed to us to be best demonstrable by the van den Bergh test. The changes have been present not only when the jaundice has been of the mildest degree, but even when no discoloration could be seen either in the skin or in the conjunctiva. These subicteric conditions are commonly present in the absence of gross obstruction in the hepatic or common ducts and seem to indicate changes in the hepatic cell itself. Physiologically, hepatic cell change seems to be synonymous with obstruction of the capillary ducts, the hepatic cell is the only structure present which could cause obstruction of these ducts, this seems to be true from clinical observa-

tions and has been demonstrated experimentally. In this respect the status of the van den Bergh test has acted as an indicator of the state of function of the hepatic cell.

In the cases included in this study, biliary tract disease was constituted primarily by calculus-producing conditions either in the absence of, or associated with, infection. The lithiasis which results from disturbance of the cholesterol metabolism practically always originates in the gallbladder and is primarily free from the influences of bacterial infection, the absence of the latter symptoms are due to the attempted or consummated passage of stones, as foreign bodies from the gallbladder, in such cases we have no clinical evidence that reflex disturbances have occurred in the hepatic cell. The latter disturbances occur only under three conditions (1) when infection is added, (2) when obstruction occurs and (3) when both of these complications exist together. The variations of the van den Bergh test that we have obtained, when either or both of these two factors have been added have indicated that in their presence disturbances of hepatic function frequently occur.

The presence of stones in the biliary ducts—especially the hepatic and common bile ducts—interferes with the free passage of bile into the intestine. The difference between the effects of the latter and of a complete obstruction is only one of mathematical proportion. An important item to remember is that infection is frequently present with a nonobstructive or obstructive stone in the duct system. An important deduction of this study has been that the presence of stones in the duct system must be productive of some interference in physiologic function (case 94). This possibly accounts for some of the wide variations in the nitrogen bodies in the blood present before any operative intervention and explains the apparent inability to classify these figures properly. In any case these may seem to be of little or no clinical importance for the moment, owing to the compensatory activity of the liver and associated organs. This functional inhibition is comparable to that demonstrable in the urinary apparatus under similar calculus conditions as shown by the excretion of indigo carmine, in the latter however the happy incidence of a bilateral organ in the presence of a unilateral disease facilitates a more accurate determination of functional change by comparisons of the affected and the sound sides.

The changes in the van den Berg test and the status of nitrogen bodies in the blood in cases in which infection and obstruction were factors are shown in tables 5, 6 and 7.

6 Evidence of renal damage has been present frequently. It was present in eighteen of twenty-eight cases. The clinical and laboratory facts have suggested the following classification:

(a) In most of these instances the renal damage as a preexisting condition was mostly a laboratory phenomena and did not have any apparent relation to the primary biliary tract or secondary hepatic cell lesion

(b) In 33 per cent of the cases the renal damage was associated with jaundice. Undoubtedly in a few of these the renal lesion was independent of the pathologic condition of the biliary tract or hepatic cell as described

TABLE 5—*Effect of Mild Forms of Infections on Hepatic Functions*

Case No	Age	Van den Bergh Estimations	Urea Nitrogen	Nonprotein Nitrogen	Uric Acid	Creatinine	Blood Cholesterol
34	32	1 120000	15.4	35.8	2.0	1.0	0.142
56	48	1 100000	14.0		2.7	1.3	0.160
58	30	1 150000	18.2	35.2	2.2	1.0	0.142
59	35	1 2000000	15.4	34.1	2.5	1.0	0.200
60		1 2000000	15.4	34.1	2.5	1.0	0.176
61	25	1 1000000	15.4	35.8	2.0	1.0	0.090
82	40	1 1500000	26.6	50.0	2.5	1.0	0.124

* Infection was indicated by the local pathologic changes and other clinical and laboratory evidence. All of the patients were somewhat jaundiced.

TABLE 6—*Effects of Severe Forms of Infection on Hepatic Function*

Case No	Infections	Van den Bergh Estimations	Urea Nitrogen	Nonprotein Nitrogen	Uric Acid	Creatinine	
91	Cholangitis with de generation	1 5000	14.0	35.0	2.8	1.3	Died
99	Cholangitis, multiple abscesses	1 5000	17.0	28.0	1.0	1.0	Died, no operation
85	Purulent cholangitis, necrosis	1 78000	18.2	31.5	3.5	1.2	Died

TABLE 7—*Status of the van den Bergh Test and the Status of Nitrogen Bodies in the Blood in Cases of Obstruction of Common Duct**

Case No	Age	Van den Bergh Estimations	Urea Nitrogen	Nonprotein Nitrogen	Uric Acid	Creatinine	Blood Cholesterol	
27	63	1 16000	14.0	33.3	2.5	1.1	0.170	
101	63	1 14000	15.4	29.3	2.5	1.0	0.136	Died
102		1 20000	12.6	33.3	2.0	1.0	0.348	
103	65	1 20000	?					Died

* All of the patients were deeply jaundiced.

in the preceding paragraph. In a few, however, the evidence seemed conclusive that the jaundice had an etiologic relationship to the renal damage. Table 8 illustrates this relationship.

In a few cases the renal damage resulted from the use of the anesthetic (ether). Probably a two-fold mechanism was operative here: there was either a primary effect on the parenchyma of the kidney, or the renal effect was secondary to a primary effect on the liver. In the case on which table 8 is based the biologic sequence included a primary hepatic effect with deep jaundice followed by secondary renal damage.

Table 9 contains the cases in which jaundice and renal damage coexisted, and shows the status of the van den Bergh test and the status of the content of nitrogen bodies in the blood

Important deductions to be made from a consideration of the renal aspect of this study include the following

(a) The severity of the renal damage was clinically not always proportionate to the depth of the jaundice. There were cases with mild jaundice in which the renal damage seemed to be excessive

(b) Nitrogen body retention does not always occur in the presence of the renal damage, this seems to follow the observations in cases of

TABLE 8—*Relationships of Jaundice to Renal Damage*

	Jaundice	Icteric Index	Urine Bile	Albumin	Casts
September 7	+		—	0	0
8	—++	1 15000	—		
16	—++	1 1600	—	0	0
11	—			0	0
14		1 1800			
15		1 17500			
21	—+	1 44000	—	vt	0
22	Operation				
25	+++		—	—	—
28		1 22000			
30		1 60000	—	ft	0
October 2	Fading rapidly	1 140000		0	0

TABLE 9—*Status of van den Bergh Test and of Nitrogen Bodies in the Blood in Cases in Which Jaundice and Renal Damage Coexisted*

Case No.	Age	Jaundice	Urine Bile	Nephritis	Van den Bergh Reactions	Urea Nitrogen	Nonprotein Nitrogen	Uric Acid	Creatinine
101	21	++	+++	—	1 40000	12.0	22.2	2.5	1.0 Died
102	63	++	+++	++	1 7000	14.0	22.2	2.5	1.1
103	38	++	++	—	1 18000	11.2	35.8	3.5	1.0
90	57	—	—	+	1 30000	22.4	52.5	2.5	1.1 Died
55	28	—	?	+	1 40000	63.0	122.5	6.5	1.3
23	22	—	—	—	1 300000		12.0	5.0	2.0

nephritis which occur in conditions unassociated with biliary tract and hepatic cell lesions

(c) Nitrogen body retention occurs in about 50 per cent of the cases in this group, here it assumes its largest proportions. There is not only a relative increase but a large absolute increase in the nitrogen bodies in the blood

SUMMARY AND COMMENT

In summing up the facts outlined in the preceding part of the paper, it appears that the biologic sequence of events of the entity that has its inception in biliary tract disease includes (1) an initial lesion in the biliary tract calculi infection (2) a primary effect on the hepatic cells leading to physiologic disturbances in the liver and (3) a secondary

effect in the renal apparatus which leads to an acute degeneration of the renal epithelium—acute nephritis (?), acute nephrosis (?)

Terminal manifestations occur in the second and in the third stages and especially after operative intervention. Death after operation cannot always be explained by surgical trauma or by the development of sepsis. Cases in which death occurs may be divided into two main classes, the chief differentiation being an outspoken kidney insufficiency. Our experiences have paralleled those of Heyd, and we have divided the first class into subgroups.

The first group is made up of patients who have been chronically jaundiced. Following operation convalescence progresses normally up to approximately the fourth or the fifth day, when a slight degree of somnolence appears. Stupor then slowly develops, and in from twelve to twenty-four hours coma intervenes. The temperature rises to 103 or 104 F. The jaundice remains unaltered or sometimes increases in intensity, but kidney function remains adequate, and there is no abnormal retention of nitrogen bodies in the blood. The condition cannot be assigned to dehydration or to bile wastage from an external biliary fistula. We believe that these are cases of liver exhaustion similar to the terminal stage of portal cirrhosis or to acute yellow atrophy of the liver.

The second group consists of those who are not jaundiced, as a rule, and who give a long history of infection of the gallbladder or biliary duct, various types of operation have been performed. The temperature rises to 104 or 105 F, with marked acceleration of the pulse. A peculiar toxemia develops with subsultus tendinum, carphologia and talking delirium. Preoperative chemical examination of the blood discloses no abnormality, and the status does not change after operation.

The second class comprises cases in which the clinical pictures presented are similar to those enumerated previously in the first class except that the evidences of renal damage are now present, that there is a distinct change in the amount and character of the urine excreted, and that there is marked retention of nitrogen-containing elements of the blood.

It is evident that a dysfunction of the liver and of the kidney are responsible for the clinical picture. From the clinical and laboratory observations that we have made, the assumption seems correct that the cases in the first class owe their manifestations to an advance of the biologic entity under discussion to the second stage, *i. e.*, liver dysfunction. Similarly, the conclusion seems correct that the cases in the second class owe their additional clinical and laboratory phenomena to an advance of the disease to the third stage, *i. e.*, renal insufficiency. The peculiar terminal toxemia which occurs presents a distressing symptom complex and is varied in its manifestations, it has been termed cholemia, because of diagnostic ignorance. Literally, cholemia means "bile in the

blood," a condition present, however, in all cases of jaundice even when toxemia is absent. Walters and William Mayo have suggested terms such as "cholemic hepatitis" or "cholemic nephritis" to indicate the existing pathologic condition. While the term 'cholemia' might be appropriately used for the conditions described in the second stage, it seems even better to drop the use of this term altogether and to employ the phrase "hepatic toxemia" to describe what actually happens. Similarly the phrase "renal toxemia of hepatic origin" might better describe the conditions in the third stage.

The physiology of the liver and the kidney are intimately and inseparably related, for the maintenance of the chemical status of the blood components and the life of the person depend on their cooperation. Any impairment of function of the one throws an added burden on the other, and if both are severely diseased, the resultant effects are obvious and manifested by changes in the chemical analysis of the urine and the blood and by the clinical course of the disease.

The liver has many functions, some of which are indirectly dependent on the cooperation of the kidney. As an organ, it is indispensable to life. Animals cannot live without the liver, if this organ is extirpated, as was done by Mann and his co-workers, death ensues within a few hours with symptoms of weakness, muscular twitchings and convulsions, often terminating in coma and occasionally accompanied by anuria. The margin of safety in hepatic disease is tremendous, as the partially ablated livers of experimental animals and the cirrhotic organs of alcoholic persons well bear witness. The margin of safety in pathologic conditions of the kidney while large, cannot be compared to that of the liver. It is highly probable that in hepatic disease some of the catabolic products of liver metabolism and the end-products dependent on its injury are not without their effect on kidney tissue. For this reason the clinical picture of uremia is often so closely associated with that of cholemia or hepatic toxemia. This was ascertained experimentally by Grudlinear, who injured the liver by tying off the left portal vein although there was a compensatory hyperplasia of the remaining healthy tissue, many of the animals succumbed with uremic symptoms, urinary examination revealing albumin and cylindroids and occasionally blood. Similarly, if the hepatic artery is experimentally ligated, necrosis of the liver results, usually accompanied by an anuria. This anuria, which is not reflex, in most cases is the result of direct toxic trauma on the kidney and of a consequent acute nephritis.

From these classic experiments, it is fair to assume that efficient kidney function is partially dependent and maintained by the unrestricted activity of a normal liver. When the liver is organically impaired so that its excretory bodies are shunted through the renal circulation the kidney invariably suffers, and when hepatic activity

ceases entirely, there is usually renal suppression, in other words, the chemical tests of kidney function in many far advanced cases of liver disease may actually mirror the efficiency of the liver. Most surgeons, in calculating the operative risk, disregard the liver as a factor because its activity cannot be judged clinically by sufficiently reliable simple tests. No one would operate in a case of nephrolithiasis without an evaluation of the stability of the kidney, but cases of cholelithiasis are considered as disease of the gallbladder and as being independent of any consequent liver dyscrasia.

One of the most important deductions from our studies has been that there is a close interrelationship between biliary tract disease (cholelithiasis, infection) and hepatic dysfunction. The corollary which follows closely is that every case carries with it potentialities for kidney damage (renal cell degeneration). The conditions and substances which cause these kidney changes are not definitely known, however, our clinical studies have brought the conviction that periods of jaundice intensify diminished renal function.

The relationship of jaundice to nephritis has always excited interest. In most cases of gallbladder disease jaundice is due to obstruction of the common duct. The bile blocked in the biliary channels is resorbed through the lymphatics and thence enters the blood stream, in which the various products, toxic and otherwise, are excreted by the kidneys. But jaundice may appear without obstruction of the common duct, it is seen in cholangitis or acute hepatitis accompanying the more severe types of gallstone disease.

In these cases, there is a big difference between dynamic and mechanical icterus. In the former, the bilirubin found in the serum is that which after its manufacture has been taken up by the blood, escaping its excretion by the liver cells. According to the researches of Eppinger, there are certain cases of jaundice in which an apparent mechanical obstruction to the flow of bile is lacking, but jaundice still exists, owing to biliary thrombi in the wider biliary ducts. In other cases these are absent, then the difficulty is said to be a disability on the part of the hepatic cell to allow the bile components to pass through.

Much pathologic evidence has been accumulated to prove that the bile pigments thus retained in the circulating blood not only mechanically plug the uriniferous tubules and interfere with their efficiency, but actually injure the epithelium of these excretory channels. Moelius, studying the autopsy material obtained from jaundiced patients, noted that the bile pigment appeared to collect in the loops of Henle and in the collecting tubules. Charin discovered the pigment in the epithelium of the malpighian corpuscles and Lichtwitz, in the kidney tubules. Examination of the urine in cases of catarrhal jaundice and in cases of marked obstruction of the common duct frequently discloses the presence

of casts. With the exception of the mechanical features of the jaundice the actual chemical damage caused by certain components of the bile cannot be denied. Cholate, a constituent of the bile when excreted through the kidney, causes damage. Werner has investigated the effects of bile pigments and bile acid salts by injecting them into animals. The latter cause a more severe reaction of the kidney. While Werner was convinced that bile acid salts were the harmful agents in animals, he felt assured that the bile pigments caused injury to the human kidney by obstructing the uriniferous tubules. However this, is open to debate because many believe that the bile acid salts are the agents harmful to kidney efficiency.

Analysis of the blood in these cases reveals a higher percentage of bile salts than of bile pigments and increase in the cholesterol. The bile salts presumably hold the cholesterol and the lecithin of the bile in solution, so that the increase of both these substances in the blood is probably protective. The increase in the bile salts leads to changes in the other organs, especially in the heart and kidneys, causing profound functional changes. In these cases the urine shows a greater concentration of bile salts than of bile. After a cholecystostomy, however, examination of the urine reveals a daily decrease in the bile salts with an increase in the amount of bile.

An important deduction made in our study is that clinically anesthetic drugs frequently intensify hepatic and renal physiologic disturbances. Colanin and Ascoli have advanced an interesting and plausible theory. The kidney is damaged and sensitized to a variable degree in exciting the toxins derived directly and indirectly from the destruction of liver tissue. The anesthesia increases the amount of liver tissue toxins until they have reached such an amount that anaphylaxis occurs resulting in a cessation of kidney function. It is evident then that not only is there a basis for kidney deficiency in many cases of cholelithiasis, but that anesthesia and operation may convert a working balance into a pathologic one.

According to Kehr, parenchymatous degeneration of the kidney caused by bile is further augmented by anesthesia and operation to such an extent that anuria may result. According to von Haberer and Stahle, jaundice as such is only an incident but previous injury to the liver with its resultant toxemia is the cause of kidney insufficiency, which becomes intensified by operation and anesthesia. The depressing effects of anesthetics on kidney function are well known. Chloroform of course is a notorious kidney poison. Colp has shown that ether in prolonged operations is not without its harmful effects although von Brunn claims that there are no observations pointing to death from parenchymatous injury due to poisoning with ether.

Our studies have inclined us to believe that in many cases these hepatic or hepatic-renal physiologic disturbances are fatigue phenomena. It seems highly probable that much abnormality can and does often occur which does not show any perceptible evidence at the bedside or in the laboratory because of the enormous compensatory powers of the liver. However, when the limit of tolerance is reached, the entire mechanism breaks down, only then is definite evidence presented to the clinician. This explains the prompt recuperation after marked physiologic disturbances, such as follows the free drainage of bile in obstructive jaundice or the injection of dextrose when the intravital mobilization of sugar is interfered with, it also explains the prompt disappearance of the signs of renal damage coincidently with improvement of the primary hepatic condition.

It is amazing that the incidence of renal suppression or anuria is not greater. The plausible explanation lies in the remarkable regenerative power of liver tissue, so that the added burden thrown on the kidney is usually not sufficient to cause it completely to suspend its activities. Ante-operative chemical examination of the blood revealing nitrogen retention should be carefully evaluated. This retention may be interpreted as indicative of severe kidney deficiency, but the question should immediately present itself as to whether the breakdown is primarily kidney, or kidney secondary to hepatic, insufficiency. A high blood urea content does not mean, however, that the physiologic condition of the liver is normal or within normal limits, because the smallest possible rests of liver tissue can call forth its manufacture from the simplest ammonia salts, and urea formation is possible just before death. But since the destruction of uric acid depends on the liver, increased amounts of uric acid are fairly characteristic of failing power of the liver, and great importance should be attached to the increase of this protein in the blood. The volume of urinary output is not of great importance, unless there is actual suppression, because it is usually dependent on the amount of fluid intake, and blood figures are altered little by changes in water balance.

Nitrogen retention in the blood is not characteristically restricted to the changes occurring in this particular group of cases of biliary tract disease. The presence of high blood figures, accompanied by changes in the kidney simply represents a series of physiologic reactions to severe forms of intoxications, not infrequently seen in other and widely different conditions, such as severe burns, various drug poisonings and high intestinal obstructions. The impression is conveyed either that some common protein toxic body becomes available in these conditions which fails to become properly detoxified in the liver and affects the kidney, or that various allied or unrelated toxic bodies are formed which because of a common mechanism or because of elimination of the liver

factor, cause secondary renal changes with which the retention of nitrogen in the blood is associated. In the cases of biliary tract disease that we have studied the jaundice seems to be the preexisting condition which is responsible for the renal damage. Unlike results which can be produced artificially in experimental work, true anuria seldom occurs in clinical practice, but all grades of renal disturbances are recognizable.

The conclusion seems certain that the cases in which retention of nitrogen in the blood is marked form but a small proportion of all cases in which renal damage occurs, and that this abnormality of the blood indicates great disturbances in the interdependent physiologic processes of the liver and the kidney. As indicated previously the clinical symptoms and the physiologic changes may indicate severe and possibly fatal lesions in the primary, *hepatic* stage of this biologic entity, in these cases retention of nitrogen in the blood is not demonstrable. The occurrence of retention and its continued progression should bring sharply to the attention of the clinician the fact that he is dealing with the terminal *renal* stage of this biologic entity—a lesion that is fatal unless the patient obtains relief from the primary condition before recovery becomes impossible.

The experiences on which the points of view and conclusions in this communication are based are derived from observations on patients admitted to the service of Dr. A. V. Moschowitz at Mount Sinai Hospital and on patients in private practice.

DERMOID CYST OF THE MEDIASTINUM*

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Dermoid cyst of the mediastinum is a rare, but definite, clinical entity. Each case observed should be reported as fully as possible, and because I have had the opportunity to study such a case and have operated successfully on the patient, I believe that a review of the literature, with conclusions as to diagnosis and treatment, will not be out of place.

From a study of the literature, I am led to believe that the only relief for the condition is surgical removal. Of the 119 cases reported, the condition has been found in the majority at autopsy. Beyer's¹ statistics show that fifty-seven, or 47 per cent, of the patients were operated on by drainage or removal. The majority of the cysts were drained and removed at subsequent operations. Of these fifty-seven cases, there was recovery in twenty-two instances, improvement in seventeen, death in twelve, and the outcome was not stated in five. This is a mortality of 22 per cent, as operative procedure is the only means by which relief can be obtained, this can not be considered a high mortality. It is not out of proportion to the chance of relief which is offered in an otherwise hopeless condition.

Dermoid cysts of the mediastinum must be differentiated from other tumors of the mediastinum and from aneurysm, tuberculosis and empyema. While pain, cough and embarrassed breathing may suggest the condition, diagnosis can be established definitely only by aspirating the tumor and finding the characteristic glycerin-like fluid, with or without hair. The yellowish fluid which contains gumous material, epithelial cells and fat droplets, is characteristic, and its physical appearance gives more information than its chemical composition.

The embryologic origin of dermoid cysts of the mediastinum is not definitely known. Scammon advances a logical explanation as follows. In the embryo, the lateral surface of the neck is indented by a series of four (paired) branchial (gills) grooves which are separated by the branchial (gills) arches. The upper part of the first of these grooves is deepened to form the external auditory meatus. The regions corresponding to the second, third and fourth grooves become deepened, forming the cervical sinuses, which soon close and disappear. Instead of disappearing, a sac of epithelium from the lower grooves may be left unobliterated in the region of the superior mediastinum. The growth from this misplaced epithelium is supposed to form the dermoid cyst.

* Read before the Pacific Coast Surgical Association, Feb 25, 1927

1 Beyer, H L. *Ann Surg* 83:577 (May) 1926

SYMPTOMS

There is no sex preponderance in the occurrence of dermoid cysts and they may be found at any age, but the symptoms usually occur between the ages of 15 and 30. The symptoms are usually caused by pressure from the growing dermoid. Increase in size with development of symptoms may follow a blow on the chest, it may occur after an acute infection producing an intrathoracic inflammatory process or it may result from the established individuality of the cyst as in other parts of the body. The onset of symptoms may be slow, the condition increasing over months or even years. Cough is the most common and persistent symptom. A glairy, mucoid material tinged with blood or great quantities of oily liquid, which may contain hair, may be expectorated. In such cases the diagnosis is evident. Hemoptysis may be alarming and may even prove fatal. Difficult breathing is usually present. Pain, especially on exertion, is described as occurring over the tumor and radiating to the arm. The slow onset is helpful in differentiating the condition from pneumonia, empyema and pleurisy with effusion and other infectious processes. In most of the cases described fever, loss of weight, loss of strength and anorexia are present.

Beye¹ says that with the typical clinical picture, it is not advisable to aspirate, but to proceed at once to perform thoracotomy. The symptoms typical of the condition, which make definite diagnosis possible are of interest equally to the internist and to the surgeon, and I wish to express appreciation of Dr. A. H. Gunderson's untiring painstaking efforts in the diagnosis of this, our first case of dermoid cyst of the mediastinum.

REPORT OF A CASE

History.—A B, a woman, aged 22, single, a telephone operator came to my office on June 19, 1926, complaining of pain in the chest and shortness of breath. Her family history was not important. Her father and mother were both living and well; no brothers or sisters had died. There was no history of tuberculosis, cancer or other chronic diseases in the family.

She had had the usual diseases of childhood but no other illness except the present one. She associated it with an illness she had had five years before when she had experienced a throbbing pain in the left elbow and shoulder and a gripping pain in the left side of the chest which she thought was pleurisy. These symptoms were more marked when she became weary, especially in the evening and she had lost weight continuously for two months. She then developed an acute illness, which was diagnosed pneumonia and which confined her to bed from July to December, 1921.

During the following summer she had had continually a sense of oppression in the chest with coughing spells which lasted three or four days and ended when she had coughed up a pint or more of grayish foul-smelling fluid occasionally tinged with blood. Her condition was diagnosed as pulmonary tuberculosis and she was sent to Mexico for treatment. While there she gained weight and felt better although she frequently had attacks of pleurisy. In

next spring she again developed a sense of oppression in the chest, which lasted two or three days at a time, and which ended when she had coughed up about one pint of fluid. Her physician aspirated her chest and removed about a pint and a half of fluid, this procedure gave her marked relief. She improved rapidly and came to Everett about two years before she consulted me. She was fairly well until a year before, when she had again felt pressure in the chest and into the left shoulder and arm, and the cough and shortness of breath on exertion had returned. She did not have fever or chills. She lost some weight, and her symptoms gradually became more marked.

Physical Examination—Examination revealed a young woman, slightly undernourished, 64 inches (162.6 cm) tall and weighing 116 pounds (52.6 Kg). She appeared a little restless and had a slight cough. There was slight prominence of the eyeballs, but no other phenomena of the eye suggestive of hyperthyroidism. The pupils were equal and reacted to light and in accommodation.



Fig 1—Roentgenogram showing the mediastinal tumor ten days before operation

the sclera was clear. Examination of the ears, nose and throat showed that they were normal. The thyroid gland was not enlarged. The chest was slender and symmetrical, though there was slightly greater expansion on the right side than on the left. There was an area of dullness over the left side of the chest, extending from above the third rib downward over the cardiac area and from 2.5 cubic millimeters outside the left mammillary line to 5 cubic millimeters to the right of the sternum. Percussion showed that the right border of the heart was 5 cubic millimeters to the right of the midsternal line. The breath sounds over the left lung were free, with an occasional rale at the third interspace. The left border of the heart could not be outlined, as the area of precordial dullness merged with that of the tumor. The sounds of the heart were regular in both rate and rhythm and free from murmurs.

The gastro-intestinal organs were apparently normal, the abdomen did not show any evidence of tenderness, and no masses were present. Examination showed that the extremities were normal. The glands were not enlarged.

The urine was normal. Examination of the blood showed hemoglobin 85 per cent, erythrocytes, 4,300,000, leukocytes, 7,600, polymorphonuclear neutrophils 61 per cent. The Wassermann reaction on the blood was negative.

Fluoroscopic examination revealed a large smooth mass in the mediastinum the shadow of which measured about 10 cm. The heart was pushed markedly to the right, 8 centimeters to the right of the midsternal line. The excursion of the right lung was good. That of the left was limited because of pressure from the tumor. The mass was well anterior.

Exploratory Thoracocentesis—The needle was inserted at the left fourth interspace, about 2 inches (5 cm) from the sternum, with the patient under the fluoroscope. The needle, after being pushed through the wall of the chest met firm resistance. It was carefully forced through the resisting area for about 1 inch (2.5 cm). Then a mucoid, glycerin-like fluid began to leak away, and 450 cc of it was removed. The patient did not experience any distress, and



Fig 2—Roentgenogram taken three months after the removal of the tumor shown in figure 1.

went to her home that evening. She was fairly comfortable for four weeks; then she returned, complaining of her old symptoms. The tumor was aspirated again, and 350 cc of fluid was removed.

The chemical analysis of the aspirated contents from the dermoid cyst showed an oily, yellow, mucoid material containing crystals of cholesterol and some squamous cells. Microscopically, it showed fat droplets (cholesterol material) and a few squamous cells, but no hair.

Operation and Course—On Aug 29 1926 the patient entered the General Hospital and on August 30, 400 cc of mahogany-brown fluid was removed; she again felt comfortable. On Sept 1, 1926 an operation was performed under procaine hydrochloride and nitrous oxide anesthesia. An incision was made on the left side from a point on the lower border of the sternum and of the second costal cartilage arching downward with a medial convexity to a point over the sixth rib, just below and outside the nipple. The breast and pectoral muscles were dissected completely from the wall of the chest and the flap was

out Three and a half inches (8.8 cm) of the sternal ends of the third and fourth ribs were removed subperiosteally, and an incision was then made through the remaining wall of the chest (intercostal muscles, perichondrium, fascia) down to a point where dense fibrous tissue was encountered. I had expected to encounter the pleura in the exposure, but fortunately the cyst had forced the pleura of the left lung laterally to such an extent that the only connective tissue encountered by the incision was the wall of the dermoid cyst.

An aspirating needle was then passed through 1 inch (2.5 cm) of fibrous tissue before 400 cc of fluid within the cyst could be aspirated. By careful sharp dissection and digital separation, a line of cleavage was found between the cyst and the left pleural sac. Separation along this line of cleavage was continued mainly by the right index finger, when digital separation became impossible, sharp dissection was continued until another line of cleavage, separable by the finger, was found. In this manner the entire cyst was freed and

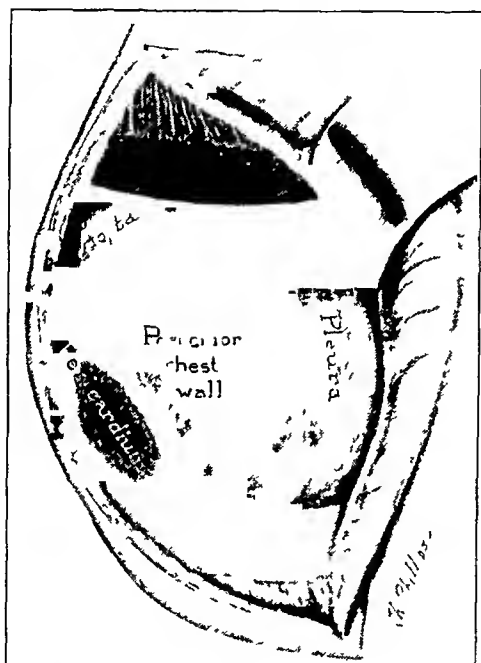


Fig. 3—Immense cavity in the mediastinum after removal of the cyst

removed from the mediastinum. Five gauze packs were placed in the cavity left by the removal of the cyst. The entire thickness of the incised chest was approximated and held in position by three retention sutures of silkworm gut. The skin was approximated with skin clips.

Gross Pathologic Observations at Operation—The cyst was $8\frac{1}{2}$ inches (21.5 cm) long and $4\frac{1}{2}$ inches (11.3 cm) at its greatest diameter, with a tapering apex. Its outer wall was composed of dense laminated, fibrous connective tissue, which was separated from the adjacent pleura and tissue of the mediastinum by a less dense and somewhat spongy layer of connective tissue. The average thickness of the wall of the cyst was one fourth of an inch (0.63 cm). In two places it was thickened by the formation of papillomatous, teatlike projections about the size of a pea, which arose from the inner wall of the cyst by a broad base. The wall of the cyst on the side next to the lung was smooth and pearly, and was almost completely covered with a brownish, caseous or salve-like deposit, about one eighth of an inch (0.3 cm) thick. The fluid within

the cyst was a dark mahogany brown. Since one point on the lining of the wall of the cyst appeared to have been the site of a recent hemorrhage, it seemed probable that the dark color of the fluid was due to a hemorrhage from this point. The cyst contained 400 cc of fluid at the time of operation. Contrary to expectations ectodermal derivatives such as hair, teeth or nails were not found in the cyst.

The patient's pulse became irregular and weak when traction was made on the cyst during its removal. One-half cubic centimeter of epinephrine was given subcutaneously, with good results. Her condition remained good otherwise throughout the operation.

Postoperative Course—Postoperative recovery was uneventful. The patient rested quietly and required little morphine. On September 3 one gauze pad was removed. Two days later the other pads were removed and consider-



Fig. 4—Patient five days after the removal of the cyst.

able serosanguinous discharge was present. The wound was clean and the patient's general condition was good though she had some difficulty in breathing and required an occasional hypodermic of morphine to relieve pain.

On September 8 the patient's progress had been favorable. Because of elevation of temperature to 102 F. she was placed in the prone position, face downward to secure better drainage and following a profuse discharge of serosanguinous material her temperature declined to normal.

On September 10 the patient was up in a wheel chair. All sutures were removed, the wound was clean and her general condition was good.

By September 18 she had been partly ambulatory for a week. She ate and slept well and breathed without difficulty. She admitted that her breathing was freer than it had been for months. The wound was clean and except for a granulating area 1 inch (2.5 cm) in diameter it was closed. She was discharged from the hospital with instructions to report at the clinic for further observation and for dressing.

On October 5, the office record showed that the wound had healed completely. The patient was feeling comfortable and well and gaining slightly in weight.

By Jan 12, 1927, she had gained 15 pounds (6.8 Kg.) in weight. She had returned to work, and said she felt better than she had for five years. She did not have any discomfort in her chest. The operative wound was firmly healed, and to all appearances the result of the operation has been a complete cure.

Pathologic Report—Sections made from the wall of the cyst showed epithelium, sebaceous glands and connective tissue.

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SUBUNGUAL MELANOMA

HUTCHINSON'S MELANOTIC WHITLOW *

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Subungual melanoma is given a somewhat inconspicuous place in the usual discussion of melanotic tumors. It appears to be a much more common lesion than the small number of reported cases would suggest. In four of the twenty-six patients with melanoma who were treated at the Barnes Hospital, the condition had its origin in the nail-bed. While Hutchinson¹ was the first to emphasize the lesion and give a lucid description of its clinical characteristics, attention had previously been given to it by other observers.² Hertzler³ has recently published a careful review of the previously reported cases, to which he adds two. Since then, Jones⁴ has described three, and Chauvenet and Dubreuilh⁵ one. I wish to add four bringing the total of reported cases up to twenty-five.

REPORT OF CASES

CASE 1—A white laborer, aged 53, was first admitted to Barnes Hospital on Nov. 5, 1915. A diagnosis of acute cardiac decompensation with auricular fibrillation and chronic valvular disease was made. He also had chronic diffuse nephritis. Following digitalization and rest in bed, he improved markedly and was discharged from the hospital. He was again admitted on Dec. 10, 1917, complaining of an ulcer of the finger. For about six years previously, he had noted a pigmented spot beneath the nail of the second finger of the left hand. This lesion had not changed in size until six months before the second admission, when, following trauma, it began to grow rapidly and finally ulcerated. There was no appreciable pain.

On admission, he presented a deeply pigmented ulcer involving the lateral side of the nail-bed, with destruction of the nail in this region. The ulcer was 1.5 cm. in diameter and was surrounded by a dusky red area extending over the entire distal phalanx. The glands were not palpable in the axillary or epitrochlear regions. Because of the cardiac condition the finger was amputated under local anesthesia without dissection of the regional lymph nodes. The patient was

* From the Department of Surgery, Washington University School of Medicine and Barnes Hospital.

1 Hutchinson. Brit. M. J. 1:491, 1889.

2 Bover, quoted from Hertzler. Gaz. med. de Par. 1854, p. 212.

3 Hertzler, A. E. Melanoblastoma of Nail Bed (Melanoma of Nail Bed). Arch. Dermat. & Syph. 6:701 (Dec.) 1922.

4 Jones, T. B. Ann. Surg. 80:839, 1924.

5 Chauvenet and Dubreuilh. Publ. chir. Soc. med. de Ch. 5:17, 1927.

Collected Cases of Subungual Melanoma

Author	Site	Age	Sex	Truama	Duration	Amputation	Course
Boyer ³	Finger	57	♂	Negative	2 years	Amputation	?
Demagnay and Mond ³	Thumb	59	♀	Negative	Several months	?	?
Annedale ³	Finger	56	?	Negative	15 months	Amputation	?
Nieberg ³	Thumb	51	♂	Positive	1½ years	Amputation	?
Willett ³	Thumb	80	♀	Negative	?	Amputation	Dead
Saen and Keser ³	Finger	62	♀	Positive	6 years	Amputation	Recurrence 3 years later in nail
Halle ³	Thumb	46	♂	Negative	7 years	Amputation	?
Hutchinson ²	?	Middle age	♂	Negative	?	Amputation	?
	Thumb	Middle age	♂	Negative	Several years	?	Recurrence in axillary glands from 8 to 10 years
Lediard ³	Finger	40	♀	Negative	2 years	Amputation	?
Fagnuet ³	Finger	63	♀	Positive	?	Amputation and axillary dissection	2 years, dead from metastases
Colcy, W B ³	Thumb	37	♂	Positive	?	Amputation	?
Trumble ³	Thumb	39	♀	Positive	2 months	Amputation	Died of local and distal recurrence
	Thumb	45	♂	Negative	6 months	Amputation	?
Murphy, J B ³	Finger	56	♂	Negative	3 years	Amputation	?
Hertzler ³	Thumb	64	♀	Positive	1½ years	Amputation	3 years later had axillary and epitrochlear recurrence
	Thumb	54	♀	Negative	4 years	Amputation	No recurrence in 2 years
Jones ⁴	Thumb	42	♀	Negative	6 months	Amputation	No recurrence in 2 months
	Toe	36	♂	Positive	2 years	Amputation	Dead 3 years later following repeated operation for recurrence
	Toe	72	♀	Positive	5 years	Amputation	Dead 3 years later from metastases
Chauvenet ⁵ and Dubreuilh	Little toe	48	♂	Negative	2 years	Amputation	Alive 1 year
Womack	Finger	53	♂	Positive	6 years	Amputation	Died with metastases 2 years afterward
	Thumb	47	♂	Positive	2 years	Amputation	No recurrence, 2 years
	Thumb	64	♂	Negative	1 year	Amputation, axillary dissection	No recurrence, 4 years
	Finger	68	♀	?	?	Amputation, axillary dissection	No recurrence, 6 months
							Dead ?

In this table ♂ indicates male ♀, female

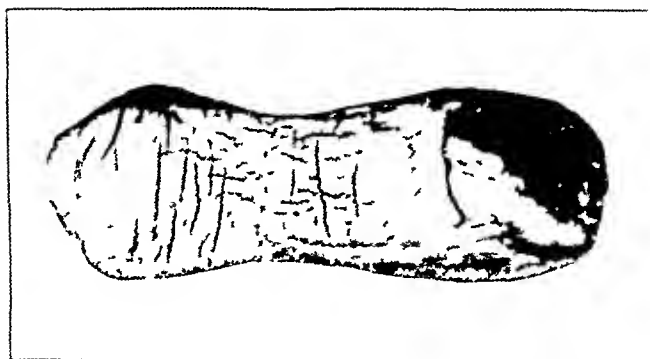


Fig. 1 (case 1) —Lateral half of the nail-bed involved by the tumor

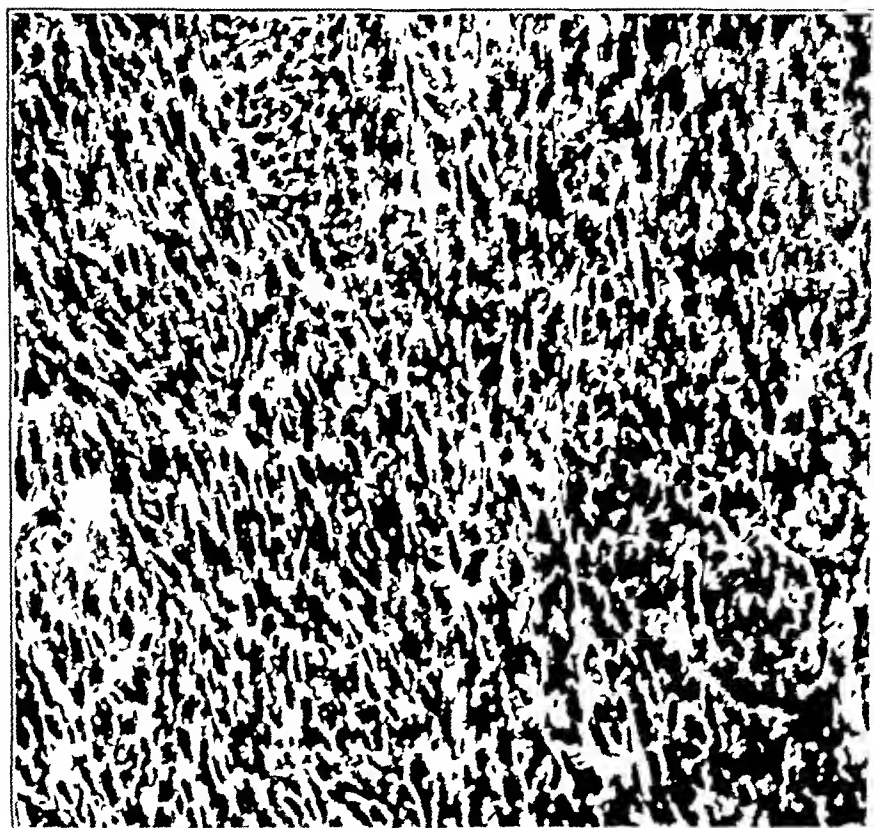


Fig. 2 (case 1) —Section taken through the base of the ulcer (Fig. 1), showing a mass of spindle cells with deeply stained nuclei. In other areas many round cells were present with more vesicular nuclei. These were more frequent in the latter area.

discharged eight days later. He was again treated at Barnes Hospital for heart disease in August, 1918, and later in January, 1919. There had not been any evidence of recurrence up to this time.

CASE 2—A white laborer, aged 47, gave a history of having mashed his right thumb in 1920. It became infected, and the nail was lost. In 1921, following slight trauma, the nail was again lost, and the nail-bed ulcerated and did not heal for some time. The patient did not note any pigmentation of the ulcer. In 1922, he struck the nail slightly with a baseball, with the same sequence of events. This ulcer did not heal, it became black and caused a slight amount of pain. He was seen at Barnes Hospital in November, 1923. At this time he presented a fungating ulcer involving the dorsum of the distal phalanx of the right thumb. There was an area in the center, about 1 cm in diameter, that was coal black, the nail was absent. The pigmented region was surrounded by a red granulating tissue that bled easily. There were palpable glands in both axillae. A roent-



Fig. 3 (case 2)—Black, fungating tumor entirely limited to the nail-bed, gray areas of necrosis are present, the result of secondary infection.

genogram of the thumb showed numerous circular, dark areas in the tuft of the distal phalanx, with questionable dissolution of the cortex at several points. The thumb was amputated at the metacarpophalangeal articulation. Axillary dissection was refused. The postoperative course was uneventful. There has not been any evidence of recurrence of the tumor up to the present time.

CASE 3—A white man, aged 64, noted a linear pigmentation in the lateral nail-bed of the right thumb in April, 1926. The distal phalanx of the thumb began to swell and to become red. Only a slight amount of tenderness was present. The nail-bed was incised by a physician, but pus was not obtained. The incision did not heal, and in its place there appeared a coal-black, granulating ulcer, which eventually involved the entire nail-bed. The patient was admitted to Barnes Hospital in February, 1927. At this time, there were no palpable regional lymph nodes. A roentgenogram of the chest did not show any evidence of metastases. The roentgenogram of the thumb showed destruction of the bone in the distal phalanx. Further examination was negative. The lymphatic glands

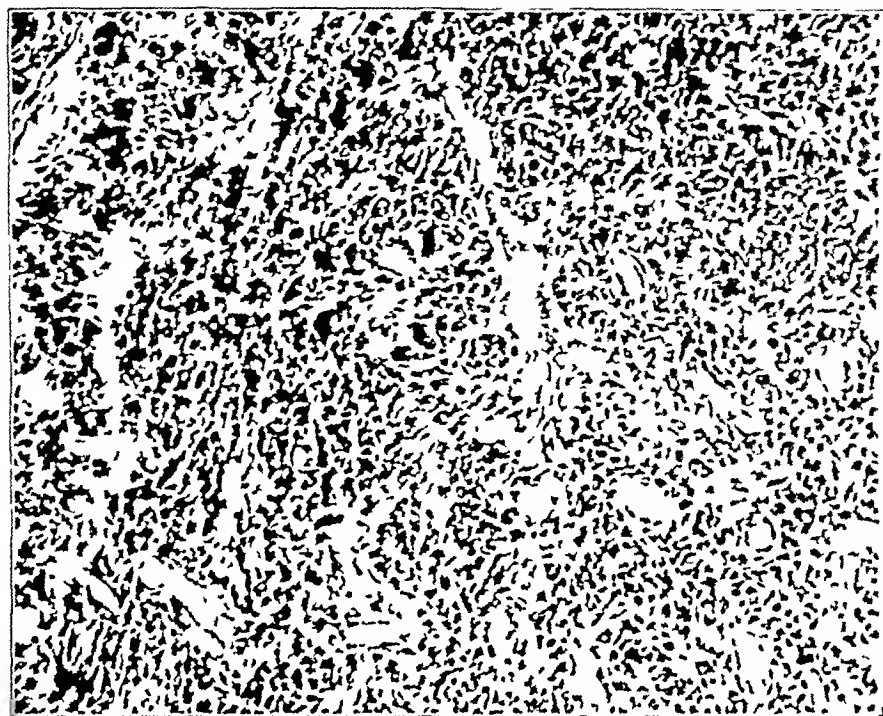


Fig 4 (case 2)—Section showing both spindle and round cells with deeply staining nuclei, only a small amount of pigment and many small blood vessels are present.

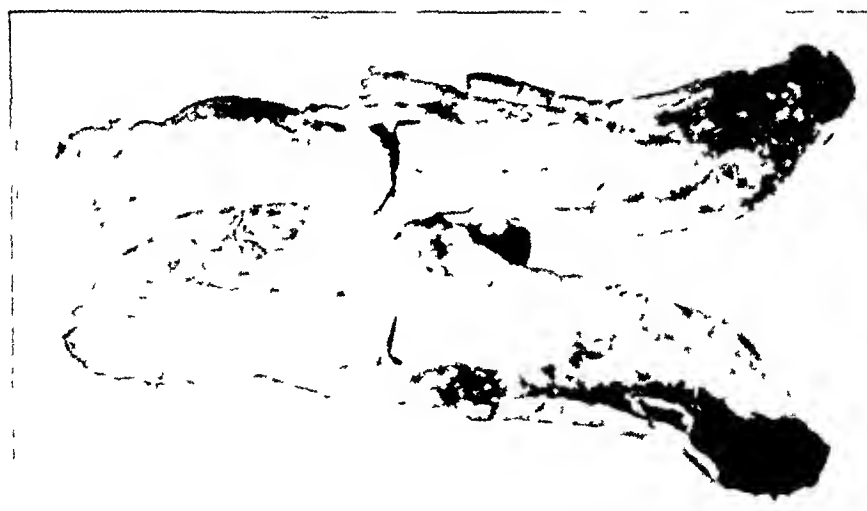


Fig. 5 (c and d) — (c) and (d) are the same as (a) and (b) but show the superimposed the growth of the Ca^{2+} and Mg^{2+} ions.

of the axilla and the antecubital fossa were dissected out, and the thumb disarticulated together with the first metacarpal bone. The postoperative course was uneventful. There has not been any evidence of recurrence in the short time that has elapsed since the amputation.⁶

CASE 4—A white woman, aged 68, had an incomplete history. The patient presented an extensive, black, fungating ulcer involving the entire finger nail-bed. The pathologic specimen was sent to this laboratory. Several large, black lymph glands were removed from the axilla in February, 1914. The patient has disappeared from observation and is presumably dead.

PATHOLOGY

Each of these patients presented a black, fungating ulcer involving the nail-bed. The ulcers, as a rule, were fairly well demarcated from the surrounding skin. It is an interesting fact that because of the black discoloration, two of the patients were first treated by other physicians for gangrene.

Microscopically, all of these cases showed two types of cells, probably representing different degrees of differentiation. The predominating cells were spindle shaped and grew in interlacing masses into the subcutaneous tissue down to the bone. The nuclei took a fairly deep stain. Mitoses were rare. Numerous areas of pigmented cells were interspersed throughout. The pigment was both intracellular and extracellular, and in several regions phagocytic cells containing pigment could be demonstrated. The other type of cell seen was polygonal or spherical and presented, relatively, many more mitoses. The nuclei were vesicular, with only a small amount of cytoplasm. Pigment was also found in these cells, but to a lesser extent than in the spindle-shaped cells.

The local lesion is limited by the fascial planes of the distal phalanx in a manner similar to that seen in infections. This phenomenon led Hutchinson to devise the term "melanotic whitlow." In many of the cases that have been reported by various observers, the lesion was first noted as a lentigo, or discoloration of the nail-bed. This may remain dormant for an extremely variable time. Subsequent extension is first by way of the regional lymphatics, metastases being first noted in the antecubital and axillary spaces before distant metastases are apparent.

PATHOGENESIS

The origin of melanotic tumors has been much discussed. The cell type has been considered epithelial, mesothelial and endothelial by different observers. The endothelial origin suggested by Reckling-

6 Since I sent the manuscript for this article to the publisher, the patient has returned with pulmonary and abdominal metastases and an enlarged gland in the posterior triangle of the neck.

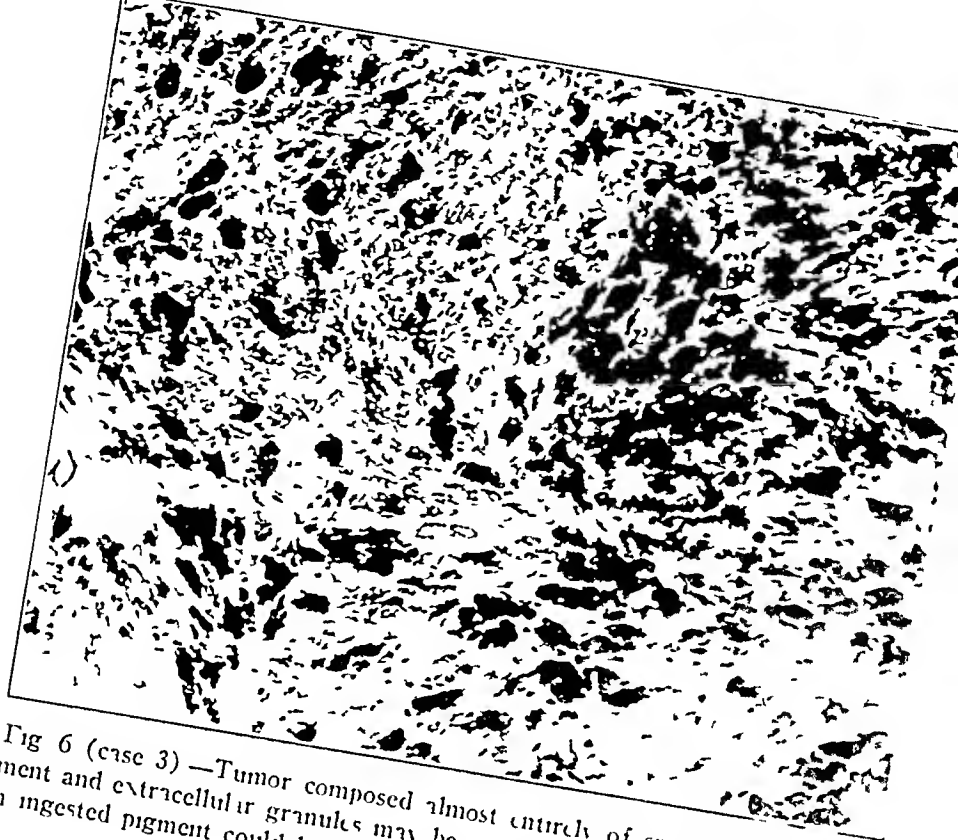


Fig 6 (case 3) — Tumor composed almost entirely of spindle cells. abundant pigment and extracellular granules may be seen. In other areas, phagocytic cells with ingested pigment could be identified. There is little stroma present.

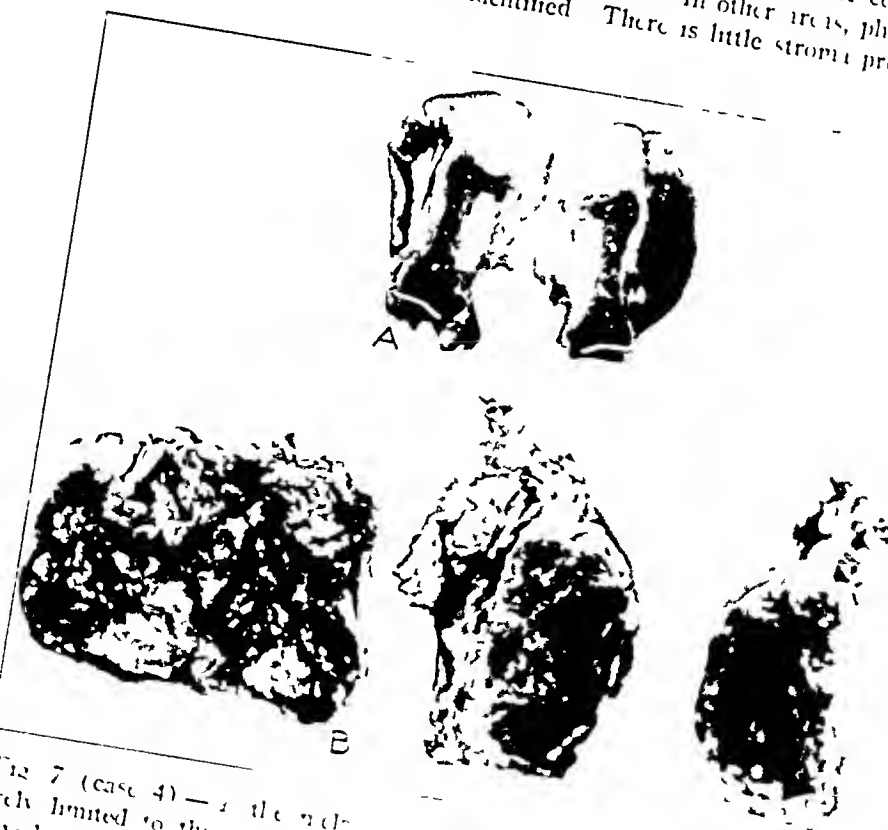


Fig 7 (case 4) — The nodules are limited to the region of the tumor. The nodules are removed from the tumor. The nodules are removed from the tumor.

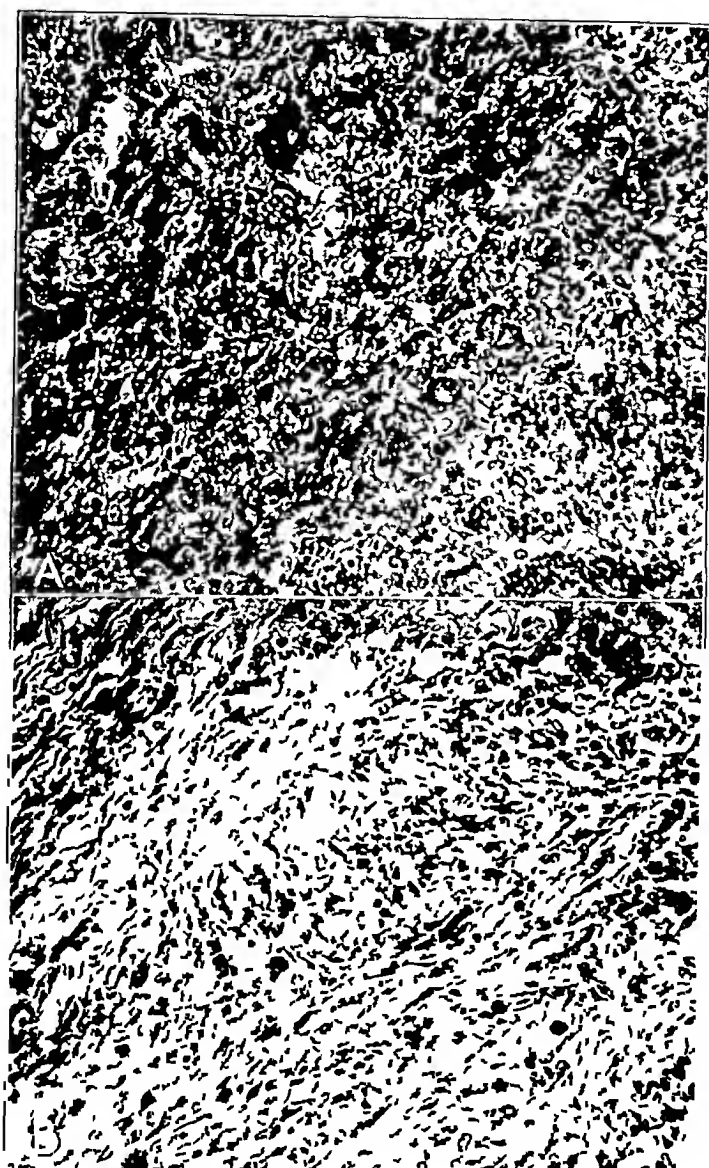


Fig 8 (case 4) —*A* shows a section taken through the primary lesion. The cellular outline is obscured by the extracellular deposits of pigment. Many leukocytes may be seen. *B* shows a section taken through the metastasis to the axillary lymph nodes. No lymphatic tissue may be seen. Both round and spindle cells are present, a few of them containing pigment.

hausen has found little support. Unna insisted on an epithelial origin while Ribbert championed that of mesothelium. The most conclusive studies, perhaps, are those of Bruno Bloch⁷ and his associates. They have been able to demonstrate a melanin-producing ferment both in melanomas and in certain normal tissues by the use of 1 per cent solution of dioxyphenylalanine as a stain. This reaction has been termed the "dopa" reaction and the enzyme "dopa-oxidase." Melanin was the only pigment found in the skin. It was formed only by cells of ectodermal origin, i. e. the basal layer of the skin, cells forming the sheath and matrix of the hair, nevus, etc. In the cornua the cells forming the Mongolian spots gave a positive reaction. A negative reaction was obtained in the shaft of the hair, the chromatophores and the deeper layers of the epidermis, especially the horny layers. Though melanin is often seen in chromatophores, it apparently is never formed there. Its presence is the result of phagocytosis of the melanin extruded by the epithelial cells, in other words, the "dopa" reaction being dependent on the "dopa-oxidase," is positive only in those cells in which melanin is manufactured. Since it is positive only in cells of epithelial origin, with the exception of the blue Mongolian spots the cell origin of which is uncertain, such growths as nevus and melanoma have been considered epithelial by Bloch and his associates.

CLINICAL COURSE AND TREATMENT

Course—Trauma is often associated with the tumor and peculiarly enough, many of the patients at first have been treated for infections. This is especially true of those lesions in which pigmentation was not marked in the beginning. When trauma has not occurred the lesion appears at first as a discoloration in the lateral nail-bed, at times resembling a hematoma. Pain is not an important feature. As the lesion progresses ulceration occurs and with it secondary infection, marked by the appearance of a pyomyeloma. Metastases are first noted in the cubital and axillary spaces. The time of appearance of metastases is an extremely variable factor. In one of Jones' cases axillary metastases were seen nine months after the initial lesion appeared, while in B. Jones' case the initial lesion existed as a pigmented area for three years before the appearance of axillary involvement. Generalized metastases usually soon follow.

The tumor is more commonly seen in persons above the age of 40 years. The nail-beds of the fingers are more frequently involved than the toes, nearly half of the reported cases being of the former type. Pigmentation appears to be a constant occurrence, but is not detectable in the early lesions first noted following trauma. It has not been reported in the colorectal type.

Diagnosis—A shallow, granulating ulcer in the nail-bed of a patient over the age of 40 should always be viewed with suspicion, especially if the ulcer does not tend to heal. This is true regardless of the history of the injury. The presence of pigment is pathognomonic. Any pigmentation in the nail-bed of a middle-aged patient should be carefully watched, whether or not ulceration is present.

Treatment and Prognosis—The treatment consists of early amputation of the phalanx with dissection of the regional lymph nodes. Most of the patients who have been observed long enough have died from the disease, however, lymphatic dissections were made in few of these cases until after metastasis had occurred, in many, local curettings were frequently performed before amputation. Because of the variability of the time before metastases occur, one cannot but feel that early complete operation would accomplish better results. There is little evidence to indicate that radiation, in the form of either radium or the roentgen ray, is of much value.

CONCLUSIONS

- 1 Fifteen per cent of all melanomas at the Barnes Hospital were found to be subungual.
- 2 These tumors are probably of epithelial origin.
- 3 Pigmented ulceration occurring in the nail-bed of a patient above the age of 40 is a frequent occurrence.
- 4 Early amputation of the phalanx with dissection of the regional lymph node is advised.

CYSTS OF THE SEMILUNAR CARTILAGES OF THE KNEE*

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Recently we studied a case of cysts of the internal semilunar cartilage which we believe contributes to the knowledge of the etiology and pathogenesis of this condition. Twenty-two cases of cysts of the semilunar cartilage have been reported since Elmer¹ described the first in 1904. Our case is the third reported case of cysts of the internal meniscus, the other two having been reported by Fisher² and by Allison and O'Connor.³

In the twenty-two cases the patients' ages varied from 16 to 55, but most of them were in the third decade. Twenty patients were men and three were women. There was a history of trauma immediately preceding the appearance of the cyst in nine cases; including ours, there was no history of trauma in five cases; in nine cases the presence or absence of trauma as a possible inciting factor was not mentioned.

REPORT OF CASES

History—I. K., aged 39, wrenched the left knee slightly on Jan. 5, 1927, he stepped out of an automobile. He experienced mild pain at the knee immediately afterward and for about six weeks. A swelling then appeared and increased progressively. Concomitantly with the appearance of the swelling the pain disappeared, and the patient was able to go about, go up and down stairs and performing the work of a chauffeur. He came to our attention because the swelling was increasing and was referred to Dr. Harry Lindstrom.

Physical Examination—On March 23, 1927, the patient was in good condition and he walked without a limp. The capsule of the knee was normal, the swelling on the left knee which was the size of a golf ball, was in the position of the internal semilunar cartilage, and was just below the line of the joint. The swelling was irregular and fluctuant, it was not sensitive and was more prominent during extension of the knee.

* From the Hospital for Joint Diseases.

¹ Elmer, A. M., *Memorial*, 3, Vol. 2, p. 51, 1907, 1908.

² Fisher, A. G., *The Knee Joint*, 1, p. 149, 1911, 1912.

The Macmillan Company, 1929.

³ Allison, N., and O'Connor, J. D., *Surg., Gynec. & Obst.*, 42, 1926.



Fig 1—Photograph taken immediately before the operation, showing bulging of the internal aspect of the knee, most prominent on full extension

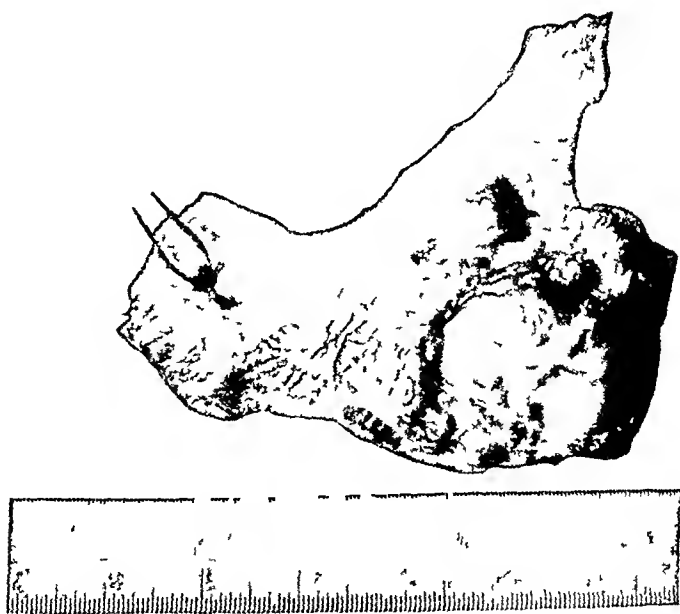


Fig 2—This photograph shows almost the actual size of the cystic internal semilunar cartilage. The suture is taken through the posterior superior end of the cartilage.

Neither of these movements was limited. There were no scars. The diagnosis of cysts of the internal semitendinous cartilage was made (fig 1).

Operation—An operation was performed on March 24, 1927, with an Esmarch tourniquet. A 4-inch longitudinal incision was made in the swelling. The cyst presented directly beneath the deep fascia.

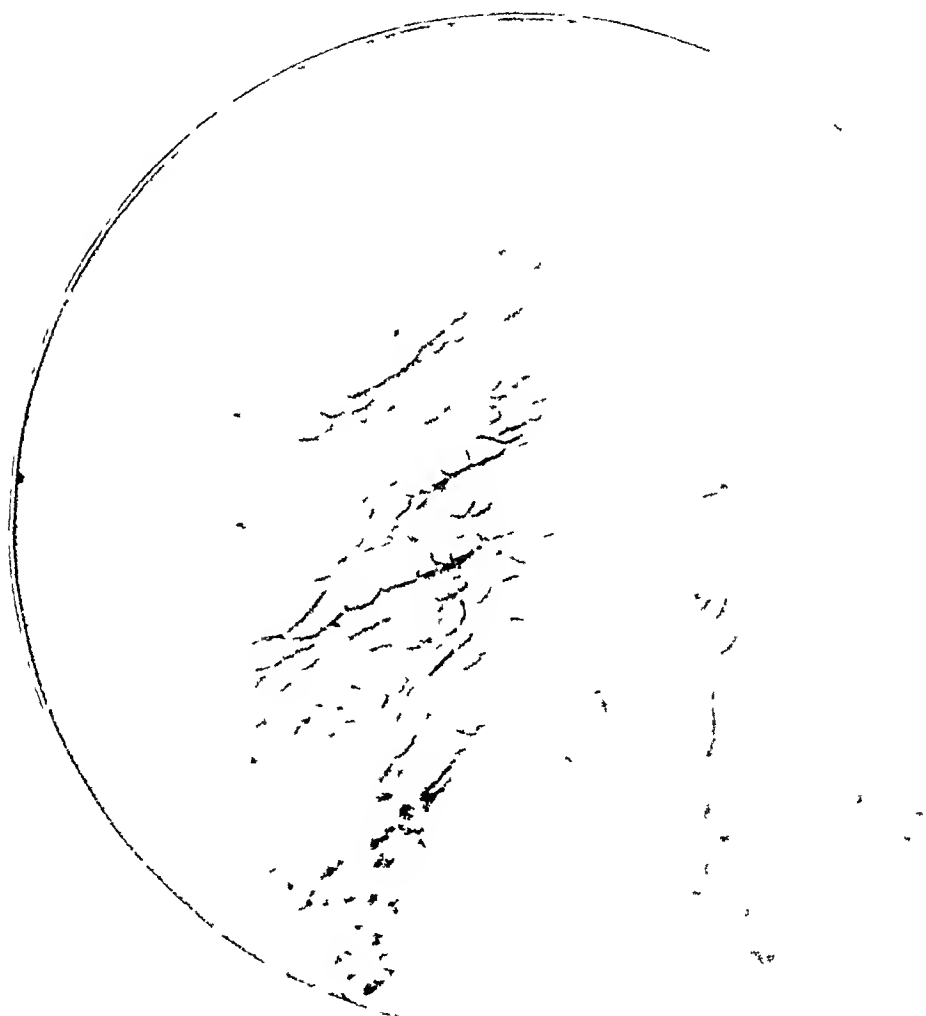


Fig. 3.—Markedly caseated. The material is soft and wide spaces appear. No cartilage is seen. The cysts of the cartilage are lined by cartilage. The cysts are filled with caseous material.

The cysts are lined by a thin layer of cartilage. The cysts are filled with caseous material. The cysts are lined by a thin layer of cartilage. The cysts are filled with caseous material.

adherent to the capsule of the joint, and strands of fibrous tissue dipped down between them at some points. The cysts contained clear, thick, gelatinous material grossly identical with the material found in ganglions. A small portion of the capsule was removed with the cysts, and the deep structures were closed with chromic catgut. The skin was closed with silk, and a light plaster of Paris bandage was applied with the knee in full extension (fig 2).

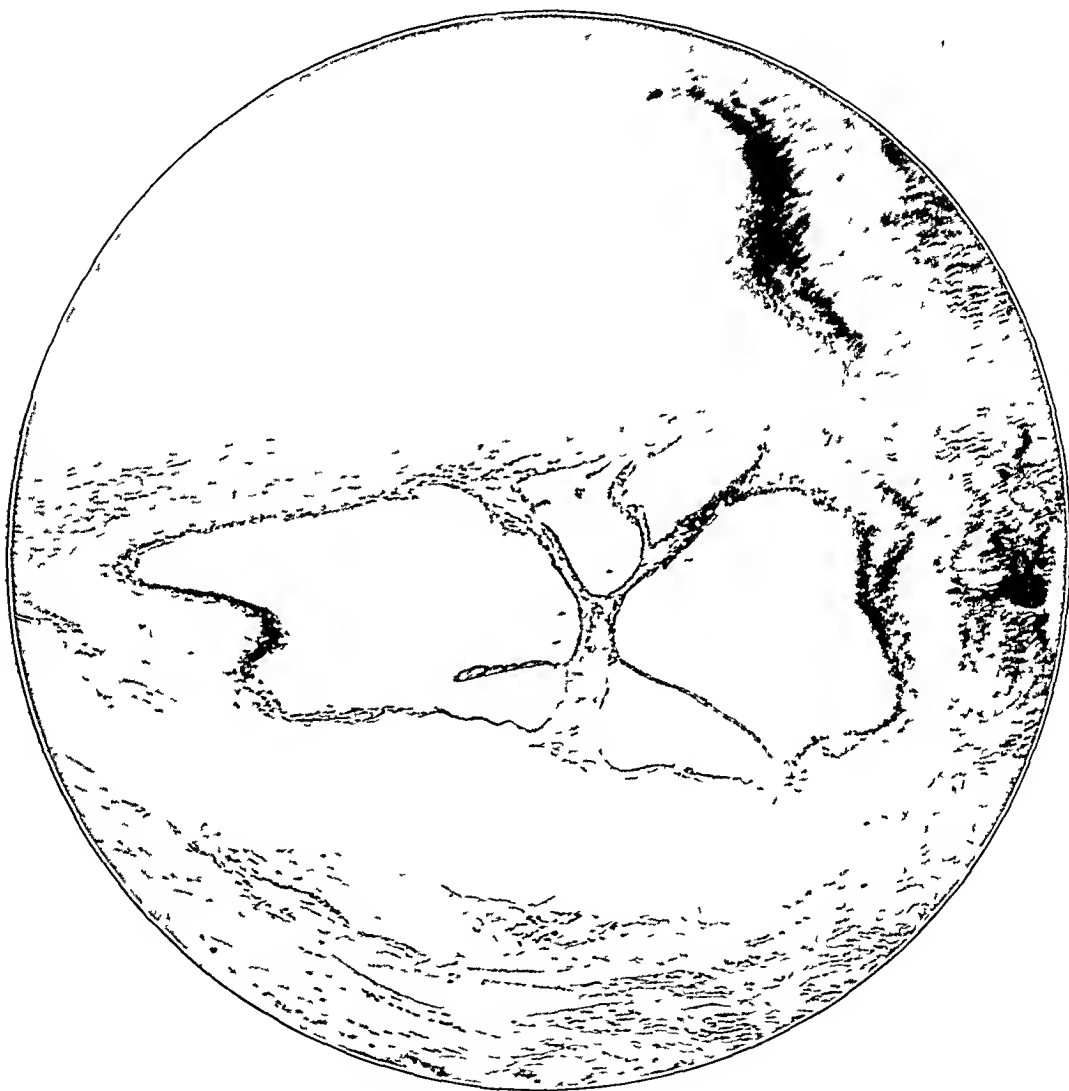


Fig 4—Multilocular cysts completely within the semilunar cartilage

Gross Pathologic Observations—The collapsed cystic left internal semilunar cartilage was roughly triangular when viewed from its upper surface. The cartilage measured about 6 cm in length along its inner free border. The cystic area, which sprang from the outer vascular portion of the cartilage, was confined mostly to its middle third, though it extended for some distance anteriorly and posteriorly. The inner avascular fibrocartilage was consequently affected, being somewhat widened and thickened posteriorly and rather smaller

than the average through the region of the main cyst. After 10 days exposure, the main cystic mass was as large as a goose egg and measured 4 by 3.5 by 1.5 cm. since some of the cysts had burst, the fluid had escaped. When the semilunar cervix was sectioned at angles to its long axis the posterior portion of the cervix was seen in the gross examination and the cut surface appeared as a white



Fig. 5—A small cyst lined by a simple cuboidal epithelium in the semilunar cervix.

translucent. The rest of the cervix was cut into sections and sectioned at right angles to the long axis. The posterior portion of the cervix was cut into sections at right angles to the long axis. The rest of the cervix was cut into sections at right angles to the long axis. The rest of the cervix was cut into sections at right angles to the long axis.

contained several small multilocular cysts within the substance of the cartilage surrounded by an edematous and, in some places, apparently necrotic cartilage. The inner avascular portion of the cartilage was thin. The next sections were made through the region of the largest cysts and showed collapsed cysts, some of which had been originally as much as 2 cm in diameter. They were separated by white fibrous septums, the intracystic surfaces of which were smooth and

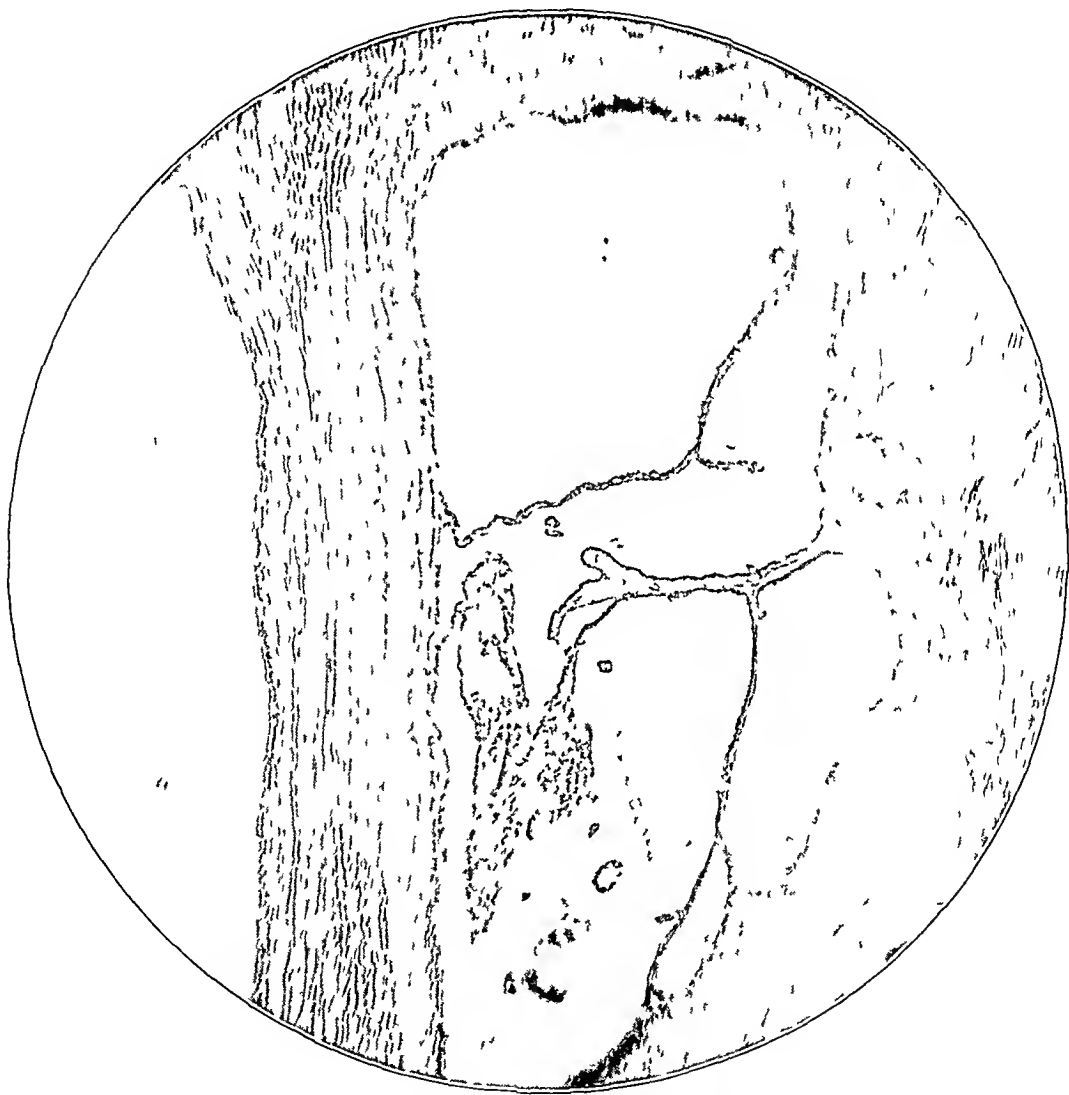


Fig 6—Small communicating synovial-lined cysts. The synovial endothelium is heaped up in one region.

shiny. These cysts communicated with each other, and as they extended laterally and upward they were applied to the internal lateral ligament and the capsule of the joint. With the accumulation of fluid, the walls had become thin. Only a fragment of noncystic semilunar cartilage remained attached to the cysts in this region. The last section, taken through the semilunar cartilage still further anterior to the main cystic mass, did not contain cysts.

Microscopic Examination—In the first section, the material was separated and fragmented and wide spaces filled with fluid were present. These spaces might have been due partly to separation of the material. Areas of necrotic fibrocartilage were seen in which the cells were not stained and the nuclei in the fibrocartilage areas were swollen, giving the cells the appearance of being circular.



FIG. 7—A cyst wall with the appearance of fibrocartilage. The endothelium of the cyst was probably the same as that of the host.

More properly, the cross section of the cyst wall is a cross section of a cyst wall. The cyst wall is composed of a layer of cells, the endothelium, and a layer of fibrocartilage.

The section of the cyst wall is shown in Figure 7. The cyst wall is composed of a layer of cells, the endothelium, and a layer of fibrocartilage.

a gradual transition from the better preserved to the necrotic cartilage, the necrotic area was not encapsulated, nor was vascularization present in the avascular necrotic cartilage. Many new vessels had appeared in the outer vascular portion of the meniscus. As in the first section, true cysts were not seen.

In the third section, the first true cyst appeared. Practically all the avascular semilunar cartilage was necrotic. The nuclei and cytoplasm did not stain.



Fig 8—The connective tissue nature of the walls through the region of the largest cysts. Vessel formation is marked in the walls, but the synovial lining is not present.

Marked edema, vacuolization and space formation were present. In about the middle of the section a large cyst occupied two low power fields. It was lined by a membrane of flattened cells, two or three rows thick. Immediately beneath this lining layer was a narrow zone of fibrillar connective tissue. Vascular fibrocartilage completely surrounded the cyst and composed the rest of the section.

Another section taken further anteriorly contained cysts of various diameters and one smaller cyst. The cysts were lined by a synovial-like membrane. There were no blood vessels in the outer zone of peripheral cartilage (fig. 4).

The fourth section also showed degenerated cartilage in the inner portion of the semilunar cartilage. In the outer portion there were many large and small communicating cysts lined by a membrane resembling synovial membrane. In some of the smaller cysts septa were present covered by the synovial-like endothelium. In other cysts septums which divided these cysts. In a few sections the same changes were seen. The cysts were all within the inner portion of the fibrocartilage and were completely surrounded by it (figs. 5, 6 and 7).

The fifth section taken from the main cystic area showed the communicating cysts some of which were from 10 to 12 mm. in diameter. In places the linings of the cysts were lined by connective tissue, but in other places the cells had become stratified, and the general appearance was more like that of synovium. Besides this endothelial layer the wall of the cysts was composed of connective tissue cells with abundant connective tissue. Some of the cyst walls contained granulation tissue with abundant inflammatory changes were not present. Only a small amount of blood was seen at the inner edge of the cysts. None of the cysts had expanded the capsule of the joint was surrounded by a dense layer of places the histologic appearance of the walls of the cysts was similar to that of chronic synovium while in other places it resembled that of granulation tissue.

The sixth section showed the same degenerative changes in the inner portion of the semilunar cartilage. There were no cysts.

Summary of Pathologic Observations.—The sections were stained and contained many cysts which were lined by a synovial-like membrane. The cysts varied in size from a few millimeters to nearly 2 centimeters. All the cysts were lined by a synovial-like layer of varying thickness. The larger cysts had expanded through the cartilage. In the outer portion of the cartilage that of a granulation. Between the cysts there was a layer of synovial endothelium which was lined by a layer of cells. All the cysts seemed to have originated from the inner portion of the semilunar cartilage and the outer portion of the cartilage. The cysts had not developed from the outer portion of the cartilage.

DISCUSSION

Many theories concerning the origin of the cysts in the semilunar cartilage have been advanced. Some have suggested that the cysts are

cysts are ganglions that arise as the result of softening and colloid degeneration of para-articular, tendinous or periosteal tissues about the knee, owing to deficient nutrition following trauma. Phemister⁵ also favors this idea, but does not believe in the primary vascular origin of the cysts or in the invariable association of trauma with the condition. He, like previous authors, did not find endothelium lining the cysts. The impression we gained from these papers was that the histologic studies were made only from the large cystic areas, which are, as we have shown, not entirely characteristic of the true nature of the cysts.

According to Fisher,² there is little doubt that these cysts are ganglions which originate in the tissues between the peripheral surface of the cartilage and the synovial membrane which covers it at this spot. Mucoid degeneration of the connective tissue takes place, in which the fibrocartilage at the periphery of the meniscus may participate.

The view maintained by Jean,⁶ Allison and O'Connor³ and Kleinberg⁷ is that the cysts represent the end-results of a degenerative process in the cartilage. According to Allison and O'Connor, a non-lacerating injury interferes with the blood supply to the cartilage and finally results in degeneration and formation of cysts. Kleinberg is in accord with this view.

Ollerenshaw⁸ was the first to find a flattened endothelium, similar to synovial membrane endothelium, lining the cysts. On the basis of this observation, he opposed the idea of degeneration cysts or of cysts following hemorrhage, and advanced the conception of their developmental origin. He believed that small endothelial nests, included in the cartilage during its development, began to secrete and became distended following trauma. Kleinberg also reported endothelium lining some of the cysts, but he believed it to be of lymphatic origin.

In our case there was no doubt about the synovial nature of the lining endothelium. Such a lining layer was found in all the smaller cysts. The larger cysts were lined in places by flattened cells which might possibly have been fibroblasts, but which were probably flattened endothelial cells because they showed gradual transitions to this type. We cannot say definitely whether these cysts resulted from congenital

5 Phemister, D. B. Cysts of External Semilunar Cartilage of Knee, *J. A. M. A.* **80** 593 (March 3) 1923.

6 Jean, G. *Bull. et mem. Soc. nat. de chir.* **1** 775, 1924.

7 Kleinberg, S. J. *Bone & Joint Surg.* **9** 323, 1927.

8 Ollerenshaw, R. *Brit. J. Surg.* **8** 409 1921.

synovial inclusions or whether they were *in situ* in the articular space. Invasion of the meniscus by synovial membrane into the cleft of the joint in the outer portion of the cartilage where it meets with the capsule. The latter consideration would seem improbable as a result of trauma or of injury in many of the cases.

Certain features in our case favor the congenital nature of the cysts. These are the multiplicity of the cysts, the presence of many synovial inclusions without formation of cysts, and the presence of recent or old hemorrhage into the cysts, our patient having been operated on within two months after trauma. The synovial inclusions become included during embryonic life, since the synovial membrane is developed in folds of synovial membrane derived from the chondrial disk. Perhaps the inclusion occurs when the capsule is torn in the outer portion of the meniscus.

It is difficult to evaluate the part that trauma plays in the formation of these cysts. About half of the cases have been attributed to trauma followed by formation of a cyst within a few days. Trauma probably leads to a rapid filling up of preformed cysts. We find no evidence to support the view which holds that the cysts are formed following tearing of the capsule and the consequent invasion by synovial membrane.

The view that the cysts follow degenerative changes in the meniscus cannot be accepted, because cysts of the semilunar capsule are also cysts. In our specimen the fibrocartilage was completely absent in the inner, avascular portion. Large tears were observed in the outer regions there was wide separation of the tissue, and the degenerated cartilage was true cyst formation, so-called, without the presence of a cyst lining. The degenerative changes are caused by the pressure exerted on the capsule, cysts are not enlarged by the pressure.

The presence of small synovial inclusions in the articular space in medium-sized cysts recalls the older literature in which it was held that they arise as the result of degeneration of the articular cartilage and the capsule of the joint. We believe that these cysts have not been reported more frequently because the older reports were made mostly from synovial inclusions in the joint space with Olfersendaw's exception. In our case the capsule was intact and the synovial membrane was not in the joint space.

As to why the cysts are found in the outer portion of the meniscus, it is not clear. The cysts are not found in the inner portion of the meniscus, except where the capsule is torn.

Received for publication

CONCLUSIONS

1 We report a case of cysts of the internal semilunar cartilage in a young man, in whom the condition became apparent several weeks after he had wrenched the knee

2 This is the third reported case of cysts of the internal meniscus

3 Cysts of the semilunar cartilage are true cysts and are lined by a synovial-like endothelium

4 We believe that the cysts are probably congenital in origin

5 Trauma is present in about half the cases and is only an initiating factor which leads to a rapid filling up of the preformed cysts with secretion

6 Cysts of the semilunar cartilage are more prominent during extension than during flexion. During flexion they can extend further into the knee joint, because more room is made for them and the capsule to which they are adherent peripherally is taut

Moynihan⁵ gives the time of occurrence of the ulcers after operation as from ten days to ten years, with the largest number of patients showing symptoms within the first year

Most authors consider a high degree of hydrochloric acid and operative trauma as the important cause of jejunal ulcer. In a report of 309 postoperative jejunal ulcers, Erchenbrecht⁶ was of the opinion that there was a primary injury of the jejunal wall from operative trauma and further corrosion by gastric juice, while Haberer and Denk⁷ have found ulcers in the line of the clamp of previous operations. They state that the mechanical factors are most important, and that the more difficult the gastro-enterostomy the more frequent is the occurrence of post-operative jejunal ulcer.

After an extensive study of 170 resected ulcers, Orator⁸ concluded that inflammation of the jejunum following gastro-enterostomy was secondary in jejunal ulcer, that in addition to an unknown factor of general character in the stomach, there was a hyperplasia of the mucous membrane of the fundus, and that when the element of trauma due to clamps or too small an opening was added, chronic jejunal ulcer resulted.

According to Kausch,⁹ the amount of compression from clamps that caused injury to the mucosa was always a variable factor. He believed that the difference in the technic of the various surgeons probably explained the apparent geographic distribution of chronic jejunal ulcer in Germany and in Austria. Many authors (Roeder,¹⁰ Konjetzny,¹¹ Pauchet,¹² Woolsey¹³ and Terry¹⁴) have observed ulcers in the line of the clamp of previous operations and have considered this form of trauma as an important contributing cause.

5 Moynihan, B. *Jejunal Ulcer, Abdominal Operations*, ed 4, Philadelphia, W B Saunders Company, 1926, p 288.

6 Erchenbrecht, H P. Ein Beitrag zur Kasuistik des Ulcus pepticum jejuni postoperativum, *Beitr z klin Chir* **127** 365, 1922.

7 Haberer and Denk, cited by Kausch, footnote 9, ninth reference.

8 Orator, V. Beitr zur Magenpathologie (histologische Untersuchungen an klinischen Resektionsmaterial) *Virchows Arch f path Anat* **255** 637, 1925.

9 Kausch, W. Das Ulcus pepticum, *Handbuch der Praktischen Chir* **3** 289, 1923.

10 Roeder, C A. The Relation of Surgical Technic to Gastro-Jejunal Ulcer, *Arch Surg* **3** 622 (Nov) 1921.

11 Konjetzny, G E. Entzündliche Genese des Magen-Duodenal-geschwurs. Ein Beitrag zur Kenntnis der Ätiologie, Pathogenese, und Therapie Magen-duodenal geschwurs, *Arch f Verdauungskr* **36** 189 (Dec) 1925.

12 Pauchet, V. Ulcus jejunal post-operaire, *Bull Acad de med, Paris* **83** 527 (June) 1920.

13 Woolsey, J H. Gastro-Jejunal and Jejunal Ulcer, Cause, Diagnosis and Treatment, *S Clin N Amer* **3** 657 (June) 1923.

14 Terry, W I. Ulcer of the Jejunum following Gastro-Enterostomy, *J A M A* **75** 219 (July 29) 1920.

The most direct evidence of injury to the jejunal mucosa from clamps has been given by Coffey¹⁵. A patient, on whom he had performed a posterior gastro-enterostomy for ulcer, died from hemorrhage fifty-six hours after the operation. The operation was performed in thirty minutes. Autopsy revealed an acute lesion in the line of the clamp with erosion of a blood vessel. Coffey has also observed similar injuries of the mucosa of experimental animals which were operated on.

Ivy¹⁶ and others have reported that chronic peptic ulcer is rarely seen in the experimental animal. He found only two chronic ulcers at postmortem examinations on 850 dogs, one in an animal from which the thyroid and parathyroid had been removed, and the other in an animal in which the pancreatic duct had been ligated.

Mann and Williamson¹⁷ produced chronic jejunal ulcers in 90 per cent of the dogs on which they experimented by an extensive operative drainage of the duodenum into the ileum. More recently, Morton¹⁸ repeated this work and obtained chronic ulcers in 100 per cent of the animals, in which, he states, the operative work was done without the use of rubber-covered clamps. Ivy's¹⁹ contention is that trauma and the poor physical condition of the animals are important predisposing factors in chronic experimental ulcer. By keeping up a good state of nutrition, he obtained only a small number of ulcers, and when clamps were eliminated and a Polya operation performed, no ulcers resulted. In my laboratory experiments,²⁰ 30 per cent of the chronic jejunal ulcers were produced when Polya operation was performed with clamps and the animals were in a poor physical condition. Healthy jejunal mucosa is indifferent to gastric secretions in dogs, according to Dogliotti and Riccio²¹. They were unable to produce ulcers in dogs when the operations were done without unnecessary traction or injury to the tissues. There are, however, no recorded observations of the appearance of the mucosa in the line of the clamp soon after operation. The presence of a chronic ulcer from one to two months later is indirect proof of a possible original operative injury to the intestinal wall.

15 Coffey, R. C. A Plea for More Direct Methods in Dealing with Gastric Ulcers and Cancers, *J. A. M. A.* **57** 1034 (Sept. 23) 1911.

16 Ivy, A. C. Contributions to the Physiology of the Stomach, *Arch. Int. Med.* **25** 6 (Jan.) 1920.

17 Mann, F. C., and Williamson, C. S. The Experimental Production of Peptic Ulcer, *Ann. Surg.* **77** 409, 1923.

18 Morton, C. B. Observations on Peptic Ulcer, *Ann. Surg.* **85** 207 (Feb.) 1927.

19 Ivy, A. C. Personal communication to the author.

20 Gallagher, W. J., and Mullen, B. P. Gastric Ulcer Studies, unpublished.

21 Dogliotti, A. M., and Riccio, F. Jejunal Ulcer After Gastro-Enterostomy, *Arch. Ital. di Chir.* **10** 821 (Dec.) 1924.

EXPERIMENTAL WORK

Technic—Normal, medium sized, healthy dogs were used. After two or three operations on the same animal, some emaciation, cachexia and infection of the skin were usually present. Ether anesthesia and aseptic technic were used in all operative work. Rubber-covered stomach clamps were employed in some of the experiments. In most cases, Young's tongue clamps were used. They have smaller blades, and consist of two soft, corrugated rubber pads, 2 by 1 by 0.4 cm, held in two elliptical shaped, thin, metal rings at a distance of 3 mm from the point of application to the bowel (fig 1). These clamps are more easily applied with less unnecessary trauma. It was thought the corrugations in the rubber pads of the clamps might prevent uniform pressure. The use of smooth pads made no perceptible difference in the results.

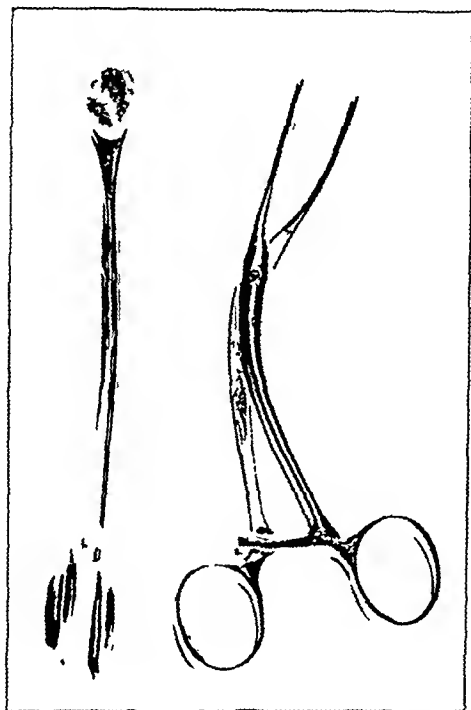


Fig 1—Young's tongue clamps used in pressure experiments on the bowel

Clamps were applied to the sites of most frequent occurrence of chronic ulcers in the stomach, duodenum and jejunum, and to other parts of the jejunum, ileum and colon for comparison. The time of application was carefully observed. The shortest time a clamp was applied was fifteen minutes, while the longest was one hour and twenty-five minutes. In addition, the length of time of the return of circulation to the clamped area was noted in all cases.

The third important factor in regard to the use of a clamp was the amount of pressure used. An accurate method of measuring this pressure was attempted through experiments with an instrument devised by Dr A J Carlson, which will be discussed later. The bowel was not clamped tightly, only sufficient pressure to produce local blanching was applied. This was assumed to represent the pressure necessary to secure hemostasis in operations on the gastro-intestinal tract (in an animal to be killed an incision was made through such a blanched area of the wall of the bowel, only a slight amount of oozing occurred). Hemostasis or a local anemia was produced by the pressures applied.

In some of the experiments, two superficially loosely tied silk sutures 1 cm on either side of the clamp, were inserted as markers.

Following operation the animals were placed on an ordinary laboratory diet of bread meat and water. There was marked disturbance of nutrition particularly following trauma to the duodenum. No attempt was made to keep the animal in a good state of nutrition since it was desired to know the influence of a poor physical condition on the production and healing of traumatic lesions of the gastro-intestinal tract.

Twenty animals were studied. In most cases from two to four experiments were performed on each animal at various times. For the sake of clearness and brevity, the experiments will be divided into four groups. In the first group the amount of pressure necessary that produced blanching of the intestine was observed in ten animals. In the second group clamps were applied to the walls of the stomach and duodenum of ten dogs. Usually two clamps were applied on different areas at the same time. In the third group the major pancreatic duct was ligated at the same time clamps were put on the stomach and duodenum. In the fourth group the application of clamps was carried out on the lower jejunum, ileum and colon.

Histologic studies were made of most acute lesions and of those areas which had healed.

Gastric analyses were made on three of the animals in group 2 before and after the clamps were applied. The dogs were given 200 cc of meat juice and a slice of bread. After from thirty-five to fifty minutes, aspirations of the stomach were made without an anesthetic.

Measurement of Pressure in Millimeters of Mercury Necessary to Produce Local Blanching in the Wall of the Intestines and in the Stomach—An instrument devised by Dr. A. J. Carlson was used (fig. 2). The apparatus consists of a rectangular metal platform in one end of which is an upright steel rod which holds a glass tube of desired length with an 8 mm bore. The lower end of the tube is covered with a rubber diaphragm. On the side of the glass tube is an extension to which is attached rubber tubing with a glass funnel, by raising or lowering this intake the height of the column of mercury can readily be varied. An adjustable millimeter ruler is attached to the side of the glass tube. The platform was set over the abdominal incision and a loop of bowel or stomach placed on the platform. The glass tube was then lowered to the margin of the bowel. By elevating the intake the mercury was increased distending the rubber diaphragm which exerted pressure on the wall of the bowel. When blanching appeared the intake was lowered until the normal color returned. By repeating this procedure the blanching point was again observed and recorded.

Even with the greatest care and by observing closely all factors it was noted that the readings varied greatly, not only in different parts of the gastro-intestinal tract, but also in the same part at varied intervals and under different degrees of anesthesia and intestinal activity.

The experiments were performed on ten dogs, three of which were killed the next day for examination of the mucosa after varied pressures of mercury had been applied for from thirty-eight to forty minutes. The remaining seven animals were used in subsequent applications of clamps.

The capillary pressure taken at the base of the finger-nail in two persons was found to be 51 and 54 mm of mercury with this instrument. Von Recklinghausen²² by a different instrument gives 55 mm

²² Von Recklinghausen cited by Howell W. H. *Textbook of Physiology*, 6th ed. Philadelphia: Saunders, 1918, p. 499.

of mercury as the capillary pressure in man at the base of the finger nail, while Danzer and Hooker,²³ by a more accurate apparatus, gives an average of 22.2 mm.

RESULTS OF EXPERIMENTAL WORK

GROUP 1—The local blanching pressures in ten dogs were observed to vary on the different parts of the gastro-intestinal tract with the degree of anesthesia and the activity of the animal. The difference in

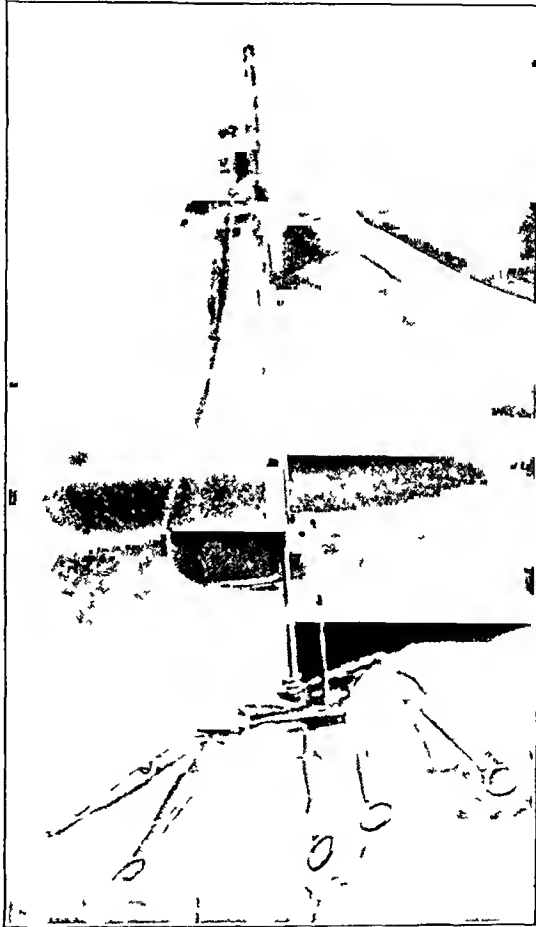


Fig. 2—Instrument used for measuring anemia pressures of the bowel in millimeters of mercury, with a loop of duodenum on the platform.

pressure is probably explained by the difference in the anatomy and the physiology of the various portions.

In dogs 18, 19 and 20, pressures in millimeters of mercury were applied to the walls of the duodenum for from thirty-eight to forty minutes, and the animals were killed the next day. There were no gross changes in the mucosa when pressure was less than that necessary

²³ Danzer, C. S., and Hooker, D. R. Capillary Blood Pressure in Man, *Am J Physiol* 52: 136, 1920.

to produce local anemia. For example, when the blanching pressure of 150 mm of mercury was applied for forty minutes in dog 19, two superficial circular areas of necrosis of the mucous membrane were found twenty-four hours later.

As the readings of capillary pressure obtained at the base of the nail in two persons were approximately the same as those found by other observers with different instruments, the high figures obtained for blanching on the bowel is partly explained by the anatomy and physiology of the different parts. Two factors of importance are 1. The intestinal lumen must be collapsed, that is, just sufficient pressure must be exerted to bring the walls together to obtain the zero point

TABLE 1—*Synopsis of Experiments of Mercury Readings on Ten Dogs in Group 1 (The Figures Indicate Millimeters of Mercury Required to Produce Anemia)*

Dog	Date	Stomach	Duode-num	Jeju-num	Colon	Time Applied	Results	Remarks
5	11/30/26		175	170	160			Light anesthesia
8	12/10/26		145	140	150			Deep anesthesia
10	12/14/26		155	150				Deep anesthesia
12	12/17/26		157	155				Deep anesthesia
14	12/23/26	161	150	140				Deep anesthesia
16	1/20/27	190	160	153	150			Light anesthesia
17	2/ 7/27	170	184	175				Light and deep anesthesia
			175	153				
18	2 ^d 8/27		160			100 mm of mercury to duode-num for 40 minutes	Normal mucosa	Anemia not produced with 100 mm of mercury
19	2/ 9/27		150			150 mm of mercury for 40 minutes	Superficial erosions 4 by 3 mm of duodenal mucosa	Anemia produced with 150 mm of mercury
20	2/ 9/27		150			75 mm of mercury for 38 minutes	Normal mucosa	Blanching not observed with 75 mm of mercury

2. The intestine must be comparatively free from activity. The presence of peristalsis will cause blanching. The resistance of the rubber diaphragm holding the column of mercury will also add a certain amount of error.

The figures obtained approximate those given by Dawson²⁴ and Burton-Opitz²⁵ for blood pressures in the large arteries of dogs. They have found the blood pressure of dogs to vary from 104 to 172 mm of mercury under various conditions. The readings, though high are fairly constant for each animal and are not intended to represent capillary pressures in the intestinal wall, but the pressures in millimeters of mercury necessary to produce grossly visible blanching as observed when clamps are applied. They are approximately the pressures used in the experiments with clamps.

²⁴ Dawson, cited by Howell (footnote 23)

²⁵ Burton-Opitz, cited by Howell (footnote 23)

Experiments on Three Dogs with Acute Duodenal Lesions—The animals studied and the method of study are inadequate for a proper appreciation of the motor or secretory activity of the stomach. It was always difficult to get the animal to eat for several days after trauma to the duodenum.

In the three animals that were studied, a delay in the emptying time of the stomach was not observed. The amount of free acid in dog 1 was decreased below that observed preoperatively, while in dog 2 and 3, there was a low degree of free acid to begin with, and an apparent increase in the acidity following trauma to the duodenum.

Dragstedt and Vaughn,²⁶ observed in dogs with experimental pyloric ulcer and Pawlow pouches that there was an increase in gastric acidity when the acid secretion was abnormally low to begin with. Ivy²⁷ has observed a delay in the emptying time of the stomach in animals that

TABLE 2—*Gastric Analyses on Three Dogs with Acute Duodenal Lesions*

Dog	Date	Pre operative Days	Post operative Days	Quantity, Cc	Free Acid Units	Total Acid Units	Time of Collection, Minutes
1	11/22/26	1		20	50	73	35
	11/30/26		7	0	0	0	35
	12/ 9/26		16	20	14	65	45
	12/13/26		20	1	0	14	45
2	11/23/26	1		57	3	25	45
	12/ 8/26		14	2	5	15	35
	12/ 9/26		15	22	13	40	50
	12/13/26		19	5	8	14	40
3	11/28/26	1		30	4	60	65
	12/ 8/26		9	4	10	72.5	40
	12/ 9/26		10	15	20	43	50
	12/13/26		14	18	48	41	40

had acute ulcer of the duodenum. This was not present in the three animals studied.

Bogendorfer,²⁸ in experiments on dogs, found that lesions of the mucous membrane of the small intestine caused a decrease in the secretion of hydrochloric acid in the stomach. In dog 1 this was found to be true, when the acidity was high preoperatively.

Ivy²⁹ states that two factors are necessary for chronic ulcer in the dog, (1) a temporary lowered body resistance, and (2) a temporary pathologic mucous membrane manifested by hypoacidity or achylia. Because of this view and Bogendorfer's²⁸ observations, a study of

26 Dragstedt, L. R., and Vaughn, A. M. Gastric Ulcer Studies, *Arch Surg* 8 791 (May) 1924.

27 Ivy, A. C. Experimental Studies on Gastric and Duodenal Ulcer, *Am J Physiol* 49 143, 1919.

28 Bogendorfer, L. Beziehungen zwischen Magensaftsekretion und Dünndarm, *Arch f Verdauungskr* 39 99 (Oct) 1926.

29 Ivy, A. C. Studies on Gastric and Duodenal Ulcer, *J A M A* 75 1540 (Dec 4) 1920.

the gastric secretion in animals with acute traumatic lesions of the duodenum was attempted. The amount of material studied, however, is too small to permit of any definite conclusions.

RESULTS OF EXPERIMENTS IN GROUP 2

GROUP 2—In the ten animals of this group it was found that no gross defects of the gastric mucosa were produced by the clamps and only a slight superficial roughness when they were applied for an



Fig 3 (dog 3, group 2) —Two acute ulcers of the duodenum seven days after pressure had been applied for one hour

hour or more. Microscopically, however, scar tissue was observed principally in the serosa and muscularis from forty-eight to sixty-two days later. In the duodenum, acute ulcers occurred in the mucosa when slight blanching was produced for thirty-two minutes, complete sloughing of the area blanched by clamps occurred when pressures were maintained over fifty minutes, leaving typical punched-out acute, perforating ulcers. Larger areas of the wall of the bowel were traumatized by rubber-covered stomach clamps than by Young's clamps.

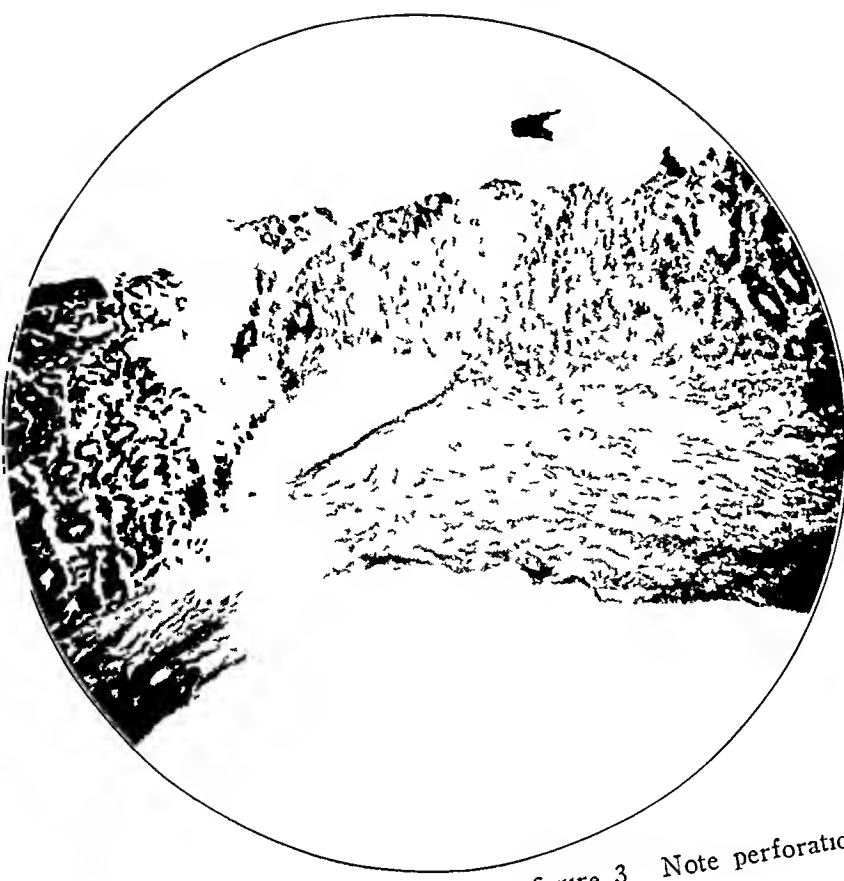


Fig 4—Photomicrograph of ulcers in figure 3 Note perforation of ulcer,
 X 60

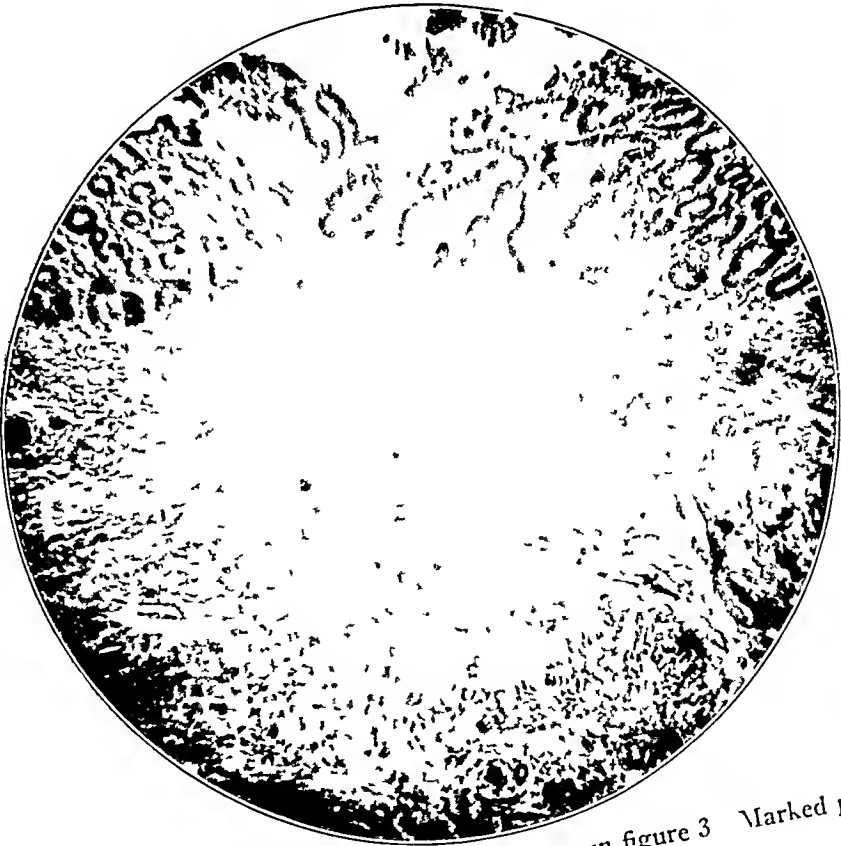


Fig 5—Photomicrograph of margin of ulcer in figure 3 Marked proliferation
 of mucosa with exudate in submucosa X 60

Experiment	Date	Operation	Duration, minutes	Return of Circulation, seconds	Interval, days		Results and Remarks	Necropsy
					1st	2d		
1	11/21/23	Young, 9 clamp applied to stomach 10 cm from pylorus lesser curvature and duodenum, 2 cm from pylorus	40	5	18		Laparotomized, no gross mucosities	
	11/24/23	Young, 4 clamp applied to stomach 10 cm from pylorus lesser curvature and duodenum, 2 cm from pylorus	50					
	11/26/23	Young, 4 clamp applied to stomach 10 cm from pylorus lesser curvature and duodenum, 2 cm from pylorus	50					

[illegible]

Acute intestinal hemorrhage and death occurred in one animal on the third day from injury to the mucosa of the duodenum when rubber-covered stomach clamps had been used. Gross injury to the duodenal mucosa was not observed when clamps were applied for fifteen minutes, microscopically, exudate, cellular infiltration and superficial necrosis of the mucous membrane were noted after twenty-four hours. In one animal with an acute duodenal ulcer, a gastric retention of twenty-four hours was observed on the seventh day. The animals were always

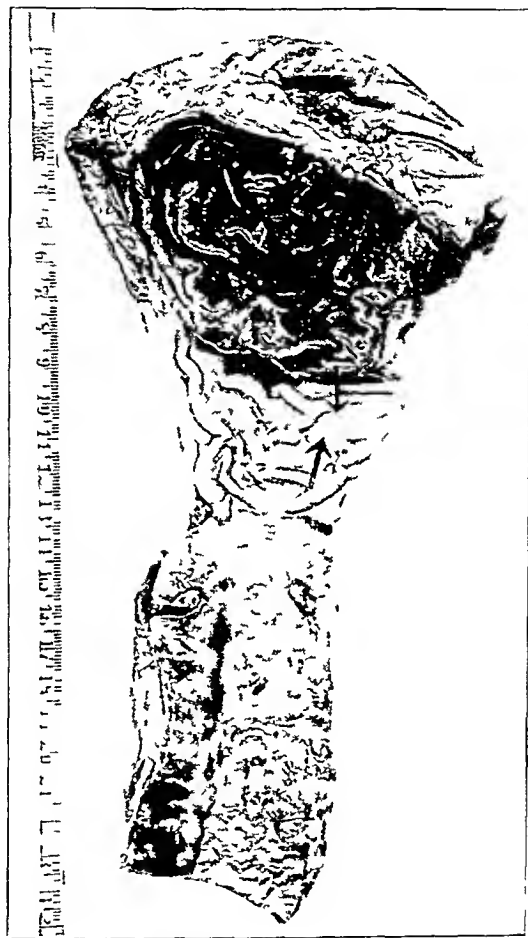


Fig 6 (experiment 7, group 2) —Acute perforating ulcers of the duodenum, five days after anemia had been produced for eighty-five minutes. Slight superficial necrosis of gastric mucosa.

acutely ill for several days following trauma to the duodenum. Vomiting was sometimes observed, but there was always a marked and rapid loss of weight, so that emaciation and infections of the skin frequently followed.

The acute ulcers of the duodenum all healed rapidly, leaving scar tissue in the area of the healed lesions. Thinning of the wall and slight dilatation were frequently found in these areas. Adhesions to

the clamped areas always occurred. In animals in a poor state of nutrition, trauma to the duodenum was always followed by a more prolonged period of illness, usually from fourteen to twenty days. There was also a slight delay in the healing time of the ulcers.

GROUP 3—In this group, the pancreatic duct of three animals was ligated with silk, and at the same time clamps were applied from thirty-three to sixty-five minutes to the duodenum and lesser curvature of the stomach near the pylorus. There was a marked disturbance of nutrition.

TABLE 4 (group 3) —*Synopsis of the Protocols of Three Dogs with Ligated Pancreatic Duct and Trauma to Stomach and Duodenum Caused from Clamps*

Experiment	Date	Operation	Duration, Minutes	Return of Circulation, Seconds	Postoperative Course and Exploratory Laparotomy	
					Interval, Days	Results and Remarks
12	12/14/26	Ligated major pancreatic duct with silk. Young's clamp applied to lesser curvature of stomach 4 cm from pylorus and to duodenum 3 cm from pylorus.	50	15	37	Sick three weeks; emaciated and skin infections present; adhesions to clamped areas; no palpable defects in mucosa.
13	2/18/27	Ligated major pancreatic duct 12/14/26. Young's clamp applied to duodenum 3 mm from pylorus.	33	Instantly	4	Vomited second day after operation; emaciated and cachectic died fourth day after operation from peritonitis, catarrhal inflammation and petechial gastritis. Mucosa, acute ulcer in duodenum nearly healed 1 by 0.4 cm near pylorus.
14	12/16/26	Ligated major pancreatic duct. Young's clamp applied to pyloric end of stomach and to duodenum 2 cm from pylorus.	50	10	20 64	Emaciated; skin infections; adhesions to clamped areas of stomach and duodenum; no palpable defects in mucosa of clamped areas.
15	2/18/27	Ligated major pancreatic duct. Young's clamp applied to duodenum, 1 cm from pylorus.	35	3	18 22	Vomited second day after operation; emaciated; skin infections; adhesions to clamped area of duodenum; no palpable defect in mucosa.
16	1/24/27	Ligated major pancreatic duct. Young's clamp applied to duodenum, 2 cm from pylorus.	65	20	14 59	Some loss of weight; appetite poor; no vomiting; animal completely recovered; nutrition good; adhesions to clamped area of duodenum; no palpable defect in mucosa.

in all the experiments of this group. When the dogs were examined from fourteen to sixty-four days after the operation, it was found that the ulcers healed rapidly with scar formation. Subsequent applications of clamps to the duodenum of these dogs were followed by a marked loss of weight and a longer period of convalescence, usually from three to four weeks. The healing time of the ulcer was also delayed. One of the animals died of peritonitis four days after the application of a clamp to the duodenum for thirty-three minutes. There was a nearly healed superficial ulcer of the mucosa. The acute ulcers of the duodenum were typical well defined punched-out lesions.

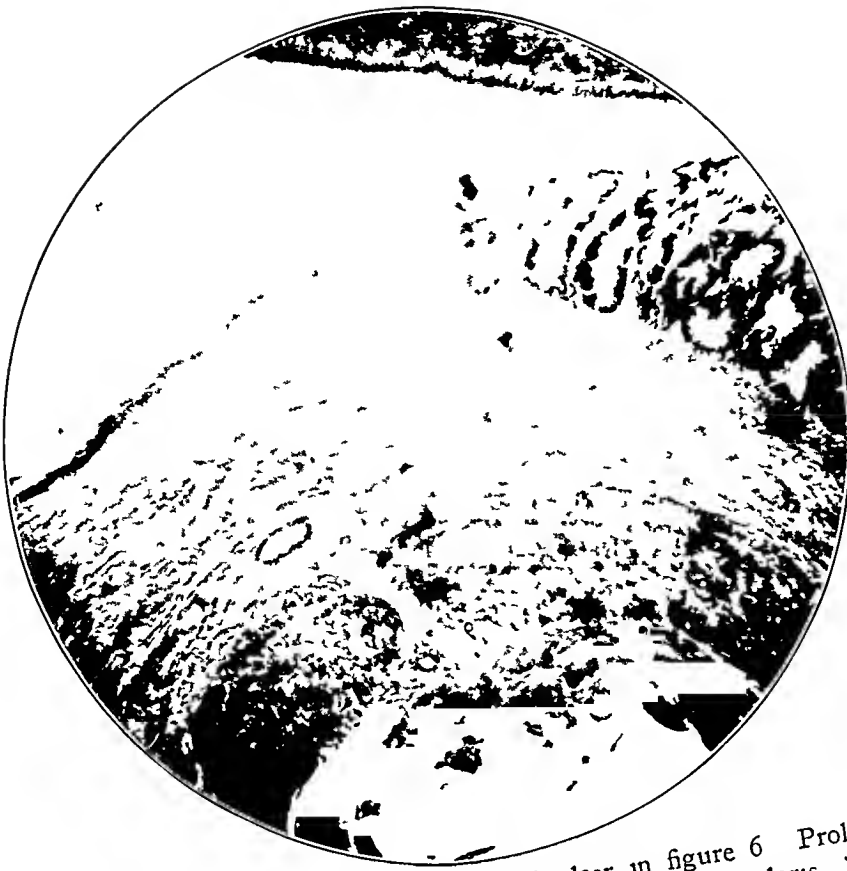


Fig 7—Photomicrograph of margin of ulcer in figure 6 Proliferation of mucosa at margin of ulcer, necrosis of submucosa and muscularis, $\times 60$



Fig 8—Photomicrograph of scars in the mucosa of the duodenum Note the mucosa inclusion in scar tissue of the submucosa and muscularis, beneath the healed ulcer, $\times 60$

GROUP 4—Six healthy dogs were used to determine the effects of trauma from clamps on those parts of the intestinal tract not directly subjected to peptic activity. The same factors of pressure and time of application were observed. Three of the animals were killed with ether anesthesia on the next day. The remaining three dogs were subjected to exploratory laparotomy and killed after seven, fifteen and thirty-one days. Gross lesions of the jejunal mucosa did not occur after

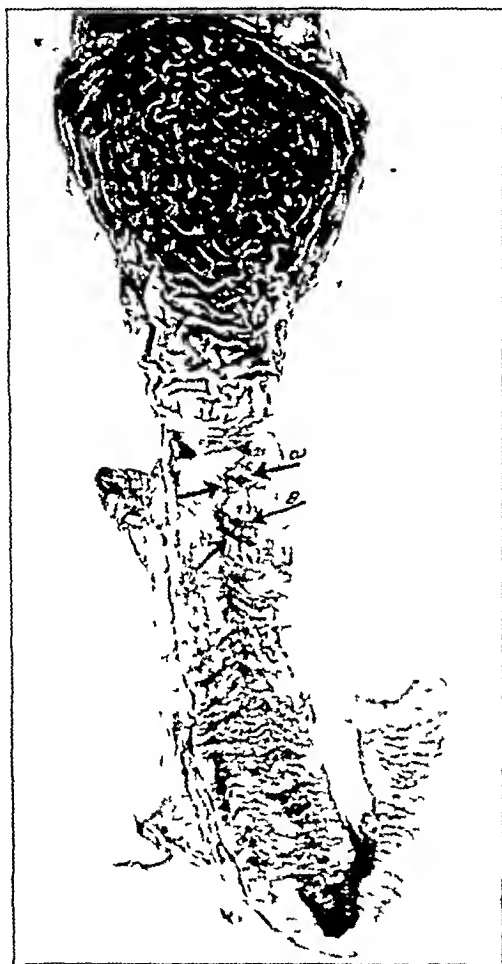


Fig 9 (dog 8, group 2) —Puckerred scar of duodenal mucosa, forty-five days after pressure had been applied for fifty minutes is indicated by *a*; an acute ulcer of the duodenal mucosa five days postoperatively, by *b*.

an application of rubber-covered stomach clamps for thirty minutes in a posterior gastro-jejunostomy, that is when the clamps were applied for coaptation and not for hemostasis. An acute ulcer developed in the midportion of the jejunum of this animal when clamps were applied forty minutes for hemostasis. The ulcer was superficial and well defined, but the base contained areas of normal mucosa and was

TABLE 5 (group 4) —*Synopsis of the Protocols of Six Dogs with Trauma to the Jejunum, Ileum and Colon Caused by Clamps*

Experiment	Date	Operation	Duration, Minutes	Return of Circulation, Seconds	Postoperative Course and Exploratory Laparotomy	
					Interval Days	Results and Remarks
17	12/17/26	Young's clamp applied to first portion and lower jejunum	50	20	31	Very sick 10 days, marked loss of weight, omentum and loop of ileum adherent to clamped areas of jejunum, no palpable defects in mucosa, mucosa of jejunum grossly normal, strands of scar tissue and few round cells in areas traumatized shown microscopically
18	12/20/26	Young's clamp applied to first and midportion of jejunum	60	15	15	No vomiting, very sick 12 days with marked loss of weight, omentum and loop of ileum adherent to clamped areas of jejunum, no palpable defects of mucosa, jejunum resected showing puckered scars at site of clamps 1 by 0.6 cm, strands of scar in all layers, especially the muscularis, also round cells shown microscopically
19	12/22/26	Posterior gastrojejunostomy, stomach clamps used for coaptation only, Young's clamp applied to midportion of jejunum	30 40	5 15	7	No defects in mucosa at site of gastroenterostomy, acute ulcer 1 by 0.8 cm and 0.1 cm deep of second clamped area, normal mucosa in center of ulcer, necrosis present, mainly at periphery of lesion marked proliferation of mucosa at margin shown microscopically
20	2/ 7/27	Young's clamps applied to lower jejunum and to first portion of ileum	50	10	1	Acute ulcer in clamped area of jejunal mucosa, 2.5 by 1 cm and 0.1 cm deep, base granular and not punched out, also two similar superficial ulcers 1.2 by 0.6 and 0.1 cm deep in mucosa of ileum
21	2/ 8/27	Young's clamp applied to ileum, 15 cm from ileocecal valve and to cecum	45	5	1	Colon tonically contracted 4 cm on either side of slightly reddened and edematous clamped area, mucosa of colon grossly normal, no changes in mucosa of ileum grossly, and only slight edema of the wall, externally
22	2/ 9/27	Young's clamps applied to midportion of ileum and descending colon	50	10	1	Slight redness and edema of wall of ileum at site of clamps and two areas, 1 by 0.4 cm and 0.1 cm deep in the mucosa, margins sharp and smooth, base red and granular, colon tonically contracted 5 cm on either side of slightly reddened and externally edematous clamped area, mucosa grossly normal

granular and hemorrhagic. On exploratory laparotomy after seven days, there were signs of rapid healing and after fifteen and thirty-one days, scarcely perceptible scars of the mucosa were noted. Microscopically, scar tissue was found in all healed lesions. In the lower jejunum, the first and midportion of the ileum, superficial areas of necrosis of the mucosa were found when clamps were applied for from forty-five to fifty minutes. In the terminal 15 cm. of the ileum an application of clamps for fifty minutes did not produce any gross evidence

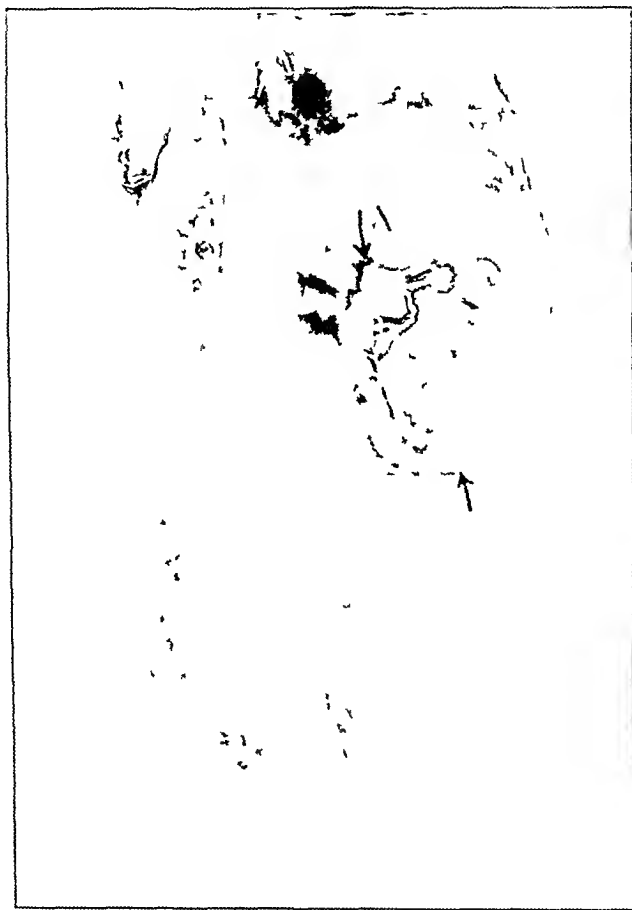


Fig 10 (experiment 9, group 2) —Sloughing of the duodenal mucosa in the clamp line of stomach clamps three days after application

of injury to the mucosa. Necrosis of the mucosa in the colon did not occur after pressure had been used as long as fifty minutes, but the colon was tonically contracted from 4 to 5 cm. on either side of the traumatized area. This condition of extreme tonicity from mechanical irritation was not observed in any other portion of the gastro-intestinal tract. The acute ulcers occurring in the lower jejunum and ileum did not have the digested out appearance of those produced in the duodenum. The local and general reaction to trauma was less marked in the lower

intestinal tract than that observed with injury to the duodenum. Convalescence was more rapid, there was no vomiting and less loss of weight. Carlson,³⁰ Luckhardt³¹ and others have observed a marked general reaction in dogs following manipulative trauma to the duodenum.

COMMENT

It has been shown in these experiments that injury to the mucosa of the duodenum and jejunum occurs from pressure at the line of the

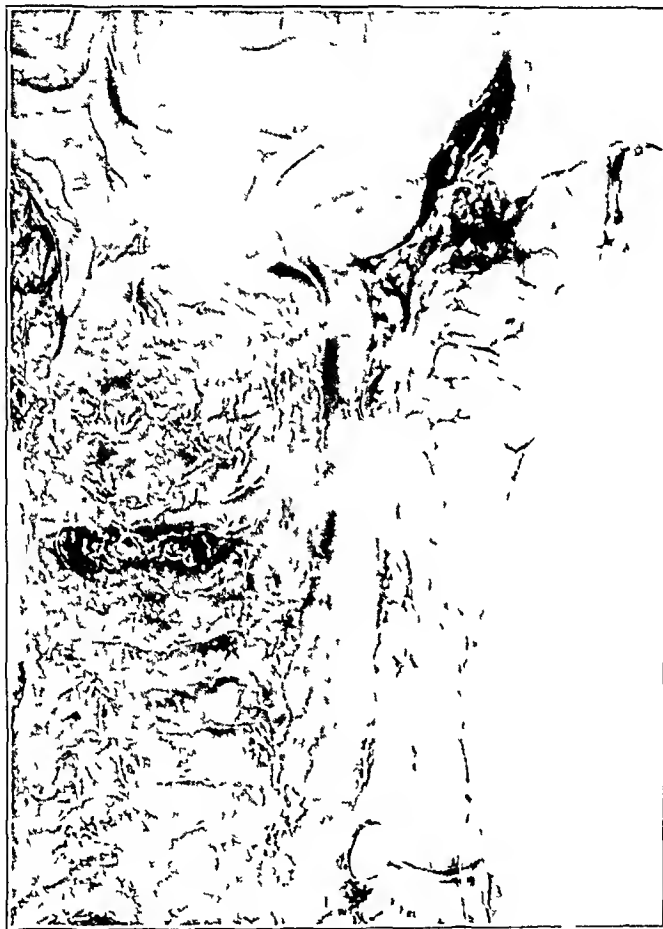


Fig 11 (experiment 11, group 2) —An acute superficial ulcer of the duodenum after anemia had been produced for thirty-two minutes, twenty-four hours post-operatively

clamp and that permanent scar tissue results from this injury, verifying the observations of many clinicians and of some investigators.

In group 2, typical acute ulcers occurred when the pressure was sufficient to produce blanching for over thirty minutes, while the pro-

30 Carlson, A J Personal communication to the author

31 Luckhardt, A B Personal communication to the author

12. Duodenum. Conva
 13. Loss of height
 14. Marked general
 15. Duodenum

to the mucosa
 the line of the

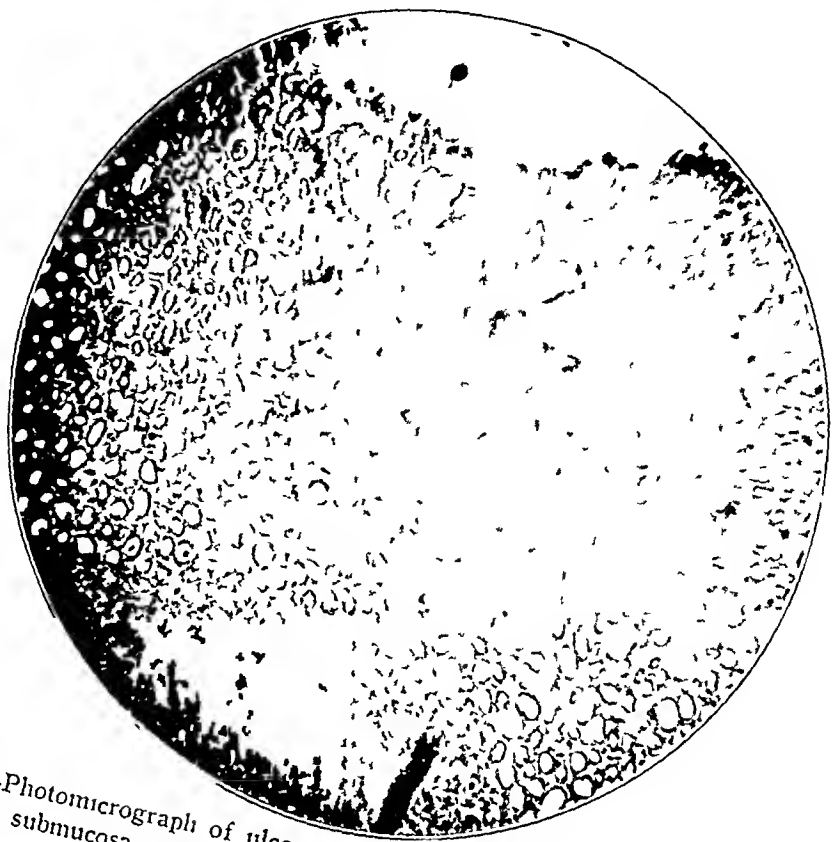


Fig 12—Photomicrograph of ulcer in figure 11, showing necrosis of mucosa
 extending to submucosa, with superficial sloughing, $\times 60$

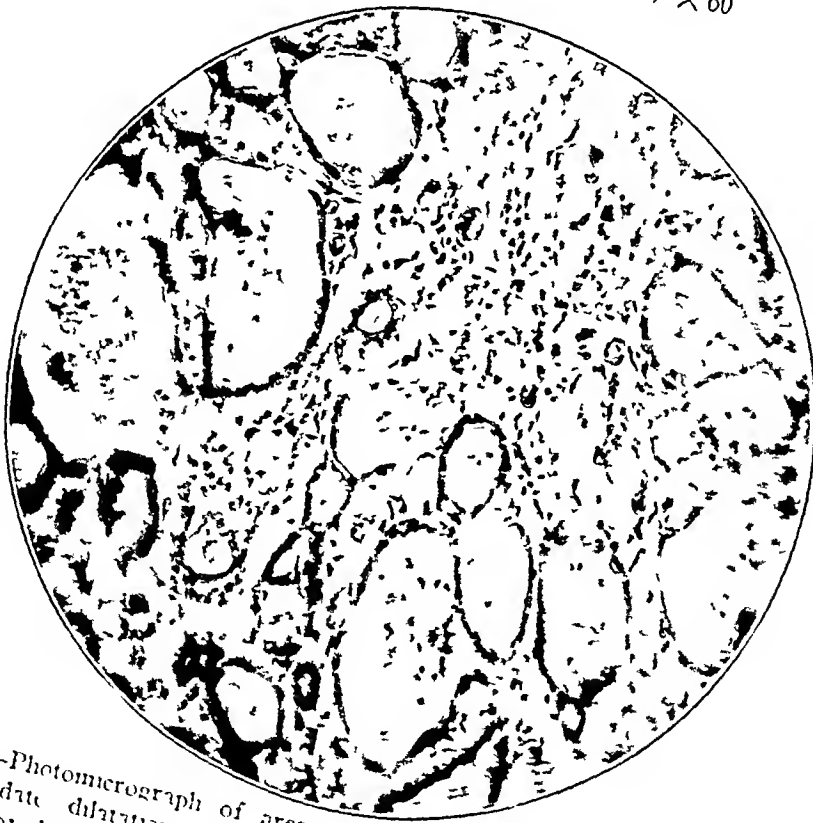


Fig 13—Photomicrograph of area near submucosa of ulcer in figure 11,
 showing exudate, dilatation of tubules of mucosa, with necrosis of cells, $\times 100$

duction of a local anemia for fifteen minutes was not followed by a grossly visible lesion of the mucosa of the duodenum or jejunum. This explains, in part at least, the opinion of Kausch⁹ that the apparent geographic distribution of postoperative jejunal ulcer was really a difference in the factor of trauma from clamps in the hands of various surgeons. It is a well known surgical fact that the element of time and the amount of compression are extremely variable. Experimentally

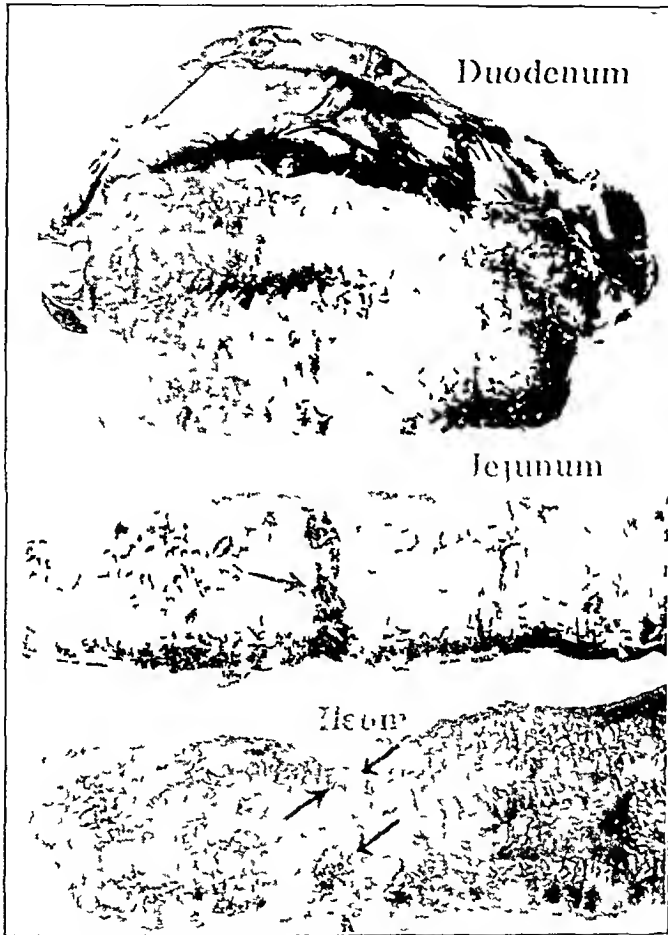


Fig 14 (experiment 20, group 4) —Normal duodenal mucosa after 100 mm of mercury were applied for thirty-eight minutes, superficial ulcer of the lower jejunum, anemia pressure applied for fifty minutes, and two superficial areas of necrosis of the mucosa of the first portion of the ileum, pressure applied for fifty minutes

it was observed that these two factors were most important in the production of acute ulcers. The acute ulcers healed rapidly, confirming the observations of numerous other investigators. Scar tissue was observed in all healed lesions, and in one case, a proliferating included portion of mucous membrane was seen in the deeper areas of the scar—

a condition observed by Wilson and McCarty³² and Spilsbury³³ in the healing of chronic peptic ulcers in man. It is reasonable to postulate that a peptic ulcer may later occur in these healed scarred areas of lowered resistance, or the acute ulcer produced by injury from clamps may become chronic when it is constantly acted on by unneutralized gastric juice. Bolton³⁴ believes that all chronic ulcers begin on an acute lesion.

The poor state of nutrition of the animal somewhat delayed the healing time, but in no case did the ulcer become chronic, verifying the observations of many other workers. The time of the return of the circulation to the clamped area bore an important relation to the incidence of acute ulcer in the duodenum and jejunum. When the color returned promptly after removal of the clamp, necrosis of the mucous membrane was superficial or entirely absent, grossly, while if the circulation was observed to return in from five to fifteen seconds, necrosis and sloughing of the mucous membrane were noted. The area of lowered resistance from the disturbed circulation was apparently digested out by the action of the gastric juice. This was observed particularly in the duodenum close to the pylorus.

In group 3, in which the major pancreatic duct was ligated, a marked disturbance of nutrition resulted. The removal of at least a part of the normal alkalinizing medium and the cachexia delayed the healing time of the ulcer and prolonged the period of convalescence. Ivy noted a delay in the emptying time of the stomach in which there were acute duodenal ulcers.

Chronic ulcers did not result in this group although Jona³⁵ reports chronic duodenal ulcers following ligation of one pancreatic duct.

The lesions produced in the lower parts of the small intestine of group 4 were always superficial and did not have the washed-out appearance of acute ulcers in the duodenum. This is probably due to the absence of the digestive action of the gastric juice since the same factors in the production of these lesions were observed in both instances.

The mucosa of the large bowel as well as that of the stomach was resistant to trauma from clamps. Acute gross injuries were not observed, although similar pressures produced acute perforating ulcers.

32 Wilson, L. B. and McCarty, W. C. The Pathological Relationship of Gastric Ulcer and Gastric Carcinoma. *Am. J. Med. Sc.* **138**: 846, 1909.

33 Spilsbury, B. H. Morbid Anatomy and Histology of Gastric and Duodenal Ulcer. *Proc. Roy. Soc. Med.* **15**: 25, 1922.

34 Bolton, Chas. Ulcer of the Stomach. *Arnold*, 1913, p. 396.

35 Jona, I. I. Experimental Study of Duodenal Ulcer. *M. J. Australia* **1**: 316 (April 19) 1919.

in the duodenum. The protective influence of a thicker musculature and a more mobile mucous membrane of the stomach and colon probably explain the absence of gross injury from clamps.

SUMMARY

The literature on the influence of trauma from clamps in post-operative jejunal and chronic experimental ulcer has been briefly reviewed.

A series of experiments on four groups has been described. In the first group a study was made of the blanching pressure in millimeters of mercury on the gastro-intestinal tract of ten dogs. It was found in these experiments that localized anemia produced for forty minutes resulted in superficial ulcers of the duodenal mucosa, while pressures less than that necessary to produce blanching for forty minutes did not result in acute ulcers. The results of these experiments were used in the application of clamps.

In the second group, ten dogs were subjected to trauma from clamps applied to the duodenum and stomach near the pylorus for from fifteen minutes to one hour and twenty-five minutes. Acute peptic ulcers were found in the duodenum when local anemia was produced for more than thirty minutes. Gross changes did not occur in the mucosa when pressure was applied for fifteen minutes, microscopically, erosions and cellular exudate were found after twenty-four hours. All of these acute ulcers tended to heal rapidly with permanent scar tissue, thinning and slight dilatation at the site of the healed lesion and with adhesions to the area externally. In the stomach, only microscopically visible changes were produced by injury from clamps, in the acute stages, superficial erosions of the mucous membrane with cellular exudate in the deeper layers and in the later stages scar tissue was present. Marked toxic reaction followed trauma to the duodenum. A poor nutritional condition of the animal resulted in a delay in the healing of the ulcer in many experiments.

A series of gastric analyses was made on three animals that had acute duodenal ulcers, a delay in the emptying time was not observed, but a slight increase in acidity was present in two dogs in which the acidity was abnormally low.

In a series of six experiments on three dogs in group 3, ligation of the pancreatic duct and trauma to the duodenum from clamps resulted in emaciation and cachexia, vomiting and a delay in the healing time of the ulcers. The scar tissue in the healed areas was not unlike that observed in group 2.

The effect of injury from clamps to the jejunum, ileum and colon was studied in six animals in group 4. Acute ulcers of the mucosa of the jejunum and first two thirds of the ileum were found. These ulcers

were superficial, healed rapidly, with the formation of scar tissue but did not have the digested out appearance of ulcers observed in the duodenum. Grossly visible injury of the mucosa of the lower ileum and colon were not noted when clamps were applied for as long as fifty minutes. A spastic condition of the colon from 4 to 5 cm. on either side of the traumatized area was found twenty-four hours later.

CONCLUSIONS

1 Typical acute ulcers of the duodenal mucosa result from the application of clamps for thirty-two minutes when the pressure applied is sufficient to produce a local anemia, if continued for longer periods of time, greater destruction of tissue results.

2 Acute ulcers produced by clamps heal rapidly with the formation of scar tissue and a moderate dilatation and thinning of the wall of the duodenum at the site of the healed lesion.

3 Trauma of the duodenum produced by clamps in animals in a poor state of nutrition with a ligated pancreatic duct produces acute ulcers which show a slight delay in the time required for healing.

4 Trauma to the duodenum in dogs causes marked local and general reactions.

5 Acute ulcers of the jejunum and upper ileum produced by clamps are superficial, heal rapidly and do not have the digested out appearance of acute ulcers observed in the duodenum.

6 The gastric mucosa and that of the large bowel are resistant to trauma from clamps.

7 From the experiments to date, it appears clear that in dogs mechanical pressure on the duodenum and the jejunum sufficient to stop the flow of blood in the compressed part for about thirty minutes induces typical acute ulcers, which on healing leave typical scars.

8 Trauma produced by clamps may be a contributing factor in the genesis of some forms of chronic experimental ulcer in dogs.

FATE OF FOREIGN BODIES IN VENOUS CIRCULATION *

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Several years ago, Sheppe¹ reported a case at the University of Virginia Hospital in which a bullet entered the abdomen and lodged in the wall of the inferior vena cava. During an attempt to remove it, the bullet escaped from the operator's fingers and disappeared. The rent in the vessel was closed. The patient reacted well from the operation, but died several days later from acute generalized peritonitis. Necropsy revealed the bullet firmly fixed near the apex of the right ventricle. Careful auscultation just before death failed to disclose any signs of cardiac disfunction.

During the World War many cases were reported in which foreign bodies, usually projectiles and shell fragments, entered a vein and later migrated to the heart. Tuffier² described a projectile, followed radiologically, which entered the right lumbar region, gradually eroded into the lumen of the inferior vena cava and six weeks later reached the right ventricle of the heart. Lyle³ reported a case in which a shell fragment entered the femoral vein in the left thigh and migrated to the heart. The patient died four days later from general gas bacillus infection evidently due to infected fibers of clothing found with the shell fragment in the right ventricle. Menett⁴ observed a projectile roentgenologically in the right ventricle for two days. It had entered the liver and worked into the vena cava, finally reaching the right ventricle. Bailey⁵ reported a most unusual case in which a toothpick was swallowed, pierced the duodenum and entered the vena cava. It was carried to the heart where it lodged in the right auricle and proved fatal by puncturing the wall of the auricle.

* From the Department of Surgery, St Elizabeth's Hospital

1 Sheppe, W M. An Unusual Gunshot Wound of the Inferior Vena Cava, J A M A **78** 1890 (June 17) 1922

2 Tuffier, T. Paris letter, J A M A **70** 1181 (April 20) 1918

3 Lyle, H H M. Migration of Shell Fragment from Right Femoral Vein to Right Ventricle of Heart, J A M A **68** 559 (Feb 17) 1917

4 Menett, F. Radiologic Observation of a Projectile in the Right Ventricle Which Had Reached There Through the Inferior Vena Cava, Bull Acad de med, Paris **79** 148 (Feb 9) 1918

5 Bailey, C H. Case of Foreign Body (Toothpick) in Heart, Arch Int Med **11** 365 (April) 1913

Grandgerard⁶ operated on a patient with a shrapnel ball in the hypogastric vein which the roentgen ray had originally shown to be in the right auricle. After the first radiosopic examination had showed the projectile in the auricle, a second examination after the patient was turned revealed the bullet in the femoral vein within Scarpa's triangle. A third fluoroscopic examination showed that the bullet had again changed its position and was then in the hypogastric vein. An operation was performed immediately and the vein was ligated around the bullet to prevent further wanderings. Birkbeck and Lormer⁷ reported a case in which a bullet entered the upper abdomen and migrated to the right ventricle. Gray removed it from the heart under local anesthesia. Death resulted four days later from multiple pulmonary infection. Le Forte⁸ on two occasions successfully removed projectiles from the cavities of the heart.

A review of the literature leaves one with the impression that wandering foreign bodies in the venous circulation are carried by the blood stream to the heart where they are kept in motion by the churning action of the heart or become entangled in the chordae tendinae of the right ventricle and gradually embedded in the endocardium. No mention is made of foreign bodies reaching the lungs. Keith⁹ stated: "There is no record of such a bullet being carried into the pulmonary artery—that is a remarkable circumstance."

EXPERIMENTS

In an effort to determine the course taken by foreign bodies in the venous circulation and their ultimate lodging place, objects of various sizes and shapes were inserted in the veins of a series of dogs. Dogs were chosen because of the size and accessibility of their veins, and the anatomic and physiologic similarity of their cardiovascular apparatus to that of man. The divisions of the right and left lungs into four and three lobes, respectively, and the less firmly fixed mediastinum in the dog, which makes intrathoracic surgery more difficult, are the chief points of difference between the heart and lungs of dog and man.

Prior to each experiment morphine was administered hypodermically. The operations were done under local or ether anesthesia. The dogs were killed by over administration of ether, by incision of the chest wall while anesthetized and by strychnine injected hypodermically.

6 Grandgerard: Rapid Migration in the Venous Network of a Shrapnel Ball in the Right Auricle. *Paris med.* **22**: 48 (Jan.) 1917.

7 Birkbeck and Lormer: Removal of Bullet from the Right Ventricle of the Heart Under Local Anesthesia. *Brit. Med. J.* **2**: 511 (Oct. 16) 1915.

8 Le Forte: Projectiles in the Heart Cavities. *Pull. Acad. Gen. & Phys.* **80**: 47 (Aug. 6) 1918.

9 Keith: A. Loose Bullets and Foreign Bodies in the Heart. *Proc. M. J.* **1**: 278 (Feb. 24) 1917.

The femoral and jugular veins were used, four different regions being thus afforded for the insertion of foreign bodies in each dog. Each vein was dissected out, ligated distally and clamped proximally with bulldog forceps. A nick was made in the wall of the vessel between these points. The foreign body was inserted in the vein, the bulldog forceps were removed and the object was pushed toward the heart by an injection of salt solution, or by the point of a clamp. The vein was then ligated proximal to the opening and completely divided between the ligatures. Considerable difficulty was experienced in the early operations owing to the disproportion between the size of the vein and the foreign bodies, and the tendency of the bullets to remain in the femoral vein and not to enter the general venous system. Later, this was overcome by dilating the vein just before inserting the bullets, and by using nails of smaller diameter and of greater length.

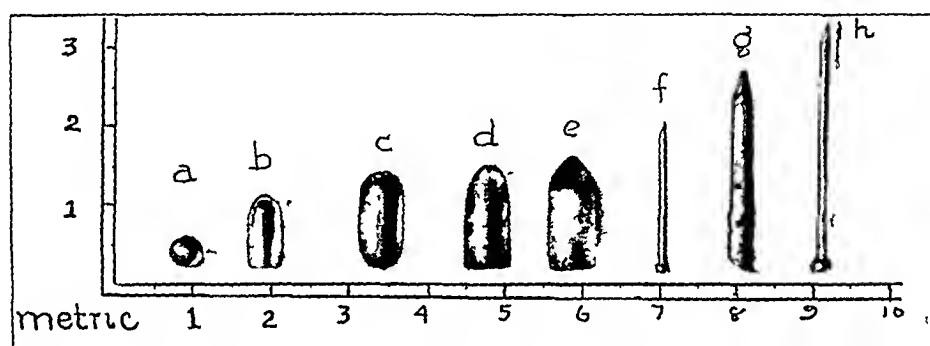


Fig 1—Types and sizes of bullets and nails introduced into veins, *a*, shot, *b*, bullet number 4, *c*, bullet number 1, *d*, bullet number 2, *e*, bullet number 3, *f*, *g* and *h*, nails and nail fragments

Sterile bullets were used at first, but later unsterile foreign bodies were introduced into the circulation in an effort to determine what difference, if any, this would make in the ultimate outcome of the experiments. These unsterile objects were not grossly septic, but they had not been sterilized prior to their insertion into the vein. With this exception the experiments were done with the usual aseptic technic observed in surgical operations. Bullets and shot of four different sizes and shapes and three types of nails and nail fragments were used in order to diversify the conditions as much as possible (fig 1).

In the earlier experiments foreign bodies of steel and lead approximating the size and shape of bullets of 5 and 6 mm caliber and varying in length from 10 to 13 mm were used. Later, shot about 4 mm in diameter and nails and segments of nails varying from 18 to 32 mm in length were used. In the first series only one foreign body was inserted in each dog at an operation, but in the later experiments several bullets

or nails were introduced at each operation. The largest number of foreign bodies were placed in dog 11 when sixteen bullets and shot were introduced during two operations.

Dog 1—On May 10, 1926, under local anesthesia one sterile number 1 bullet was inserted in the left femoral vein of a large adult female shepherd dog. The heart rate became slower and slightly irregular. No other immediate symptoms were noted.

On May 27, the roentgen ray showed a bullet in the lower lobe of the left lung.

On May 27, under ether anesthesia, two sterile number 2 bullets were inserted in the right femoral vein. No immediate symptoms were observed.

On July 1, the roentgen ray showed three bullets in the left lung.

On July 1, the dog died at the beginning of the operation owing to the over-administration of ether.

Necropsy showed that the animal was well nourished. Two bullets were found in the left lower lobe, and one in the middle lobe of the left lung. The lungs did not show any macroscopic changes. The heart and abdominal viscera were negative.

Dog 2—On May 24, 1926, under ether anesthesia, one sterile number 1 bullet was inserted in the left femoral vein of a medium sized adult female hound. No immediate symptoms were observed.

On July 6, under ether anesthesia, two sterile number 1 bullets were inserted in the right femoral vein. No immediate symptoms were observed.

On July 13, the dog was killed.

Necropsy showed the dog to be well nourished. Three bullets were found in the lungs. The lungs and heart did not show any macroscopic changes. The abdominal viscera were negative.

In the microscopic examination the lung showed areas similar to the gray hepatization stage of pneumonia. There was a slight bronchitis. The heart showed diffuse parenchymatous degeneration, with round cell infiltration.

Dog 3—On May 24, 1926, under ether anesthesia one sterile number 1 bullet was inserted in the left femoral vein of a large old male shepherd dog. No immediate symptoms were observed.

On May 27, the roentgen ray showed a bullet in the left lung.

On May 27, under ether anesthesia one sterile number 2 bullet was inserted in the right femoral vein. No immediate symptoms were observed.

On July 8, under ether anesthesia two sterile number 3 bullets and four unsterile shot were inserted in the right jugular vein. There were no immediate symptoms.

On July 11 fluoroscopic examination showed three bullets in the left lung and one bullet in the right lung.

On July 13 the dog was killed.

Necropsy showed the dog to be well nourished. Three bullets were found in the left lower lobe and one in the right lower lobe. The lungs macroscopically appeared normal. The heart and abdominal viscera were negative. There was a bullet in the right jugular vein owing to faulty insertion.

Dog 4—On June 23, 1926, under local anesthesia two sterile number 3 bullets were inserted in the left femoral vein of a large adult male shepherd dog. No immediate symptoms were observed.

On July 1 fluoroscopic examination showed the bullets in the left lung.

On July 8 the dog died of an overdose of ether administered by the operator.

Necropsy showed the dog to be well nourished. The bullets were found in the middle and lower lobes of the left lung. A dry fibrinous pleurisy corresponding to the lobes containing the bullets was present on the left side. The lungs otherwise appeared normal. The heart and abdominal viscera were negative.

Dog 5—On June 23, 1926, under local anesthesia, one sterile number 2 bullet and one sterile number 3 bullet were inserted in the right femoral vein of a medium sized adult female hound. The dog was markedly salivated immediately following the operation. This soon cleared up and no other symptoms were noted.

On July 1, fluoroscopic examination showed the bullets in the left lung.

On July 8, under ether anesthesia, one sterile number 1 bullet and seven unsterile shot were inserted in left femoral vein. It was impossible to force the foreign bodies up the femoral vein. A low midline abdominal incision was made and the bullet and shot were massaged upward. No immediate symptoms were observed.

On July 12, the dog was killed.

At necropsy three bullets were found in the left lung. The lungs did not show any gross changes. One shot was found in the apex of the right ventricle at the base of the chordae tendinae. The heart otherwise appeared normal. There were several enlarged mediastinal lymph nodes which were removed for microscopic examination. Six shot failed to leave the femoral and iliac veins owing to faulty insertion.

Microscopic examination revealed a moderate amount of fibrosis with round cell infiltration in the lungs, resembling a resolving pneumonia. There was a slight thickening of the pleura. Sections made of the heart near the site of the shot showed cloudy swelling with occasional round cells and moderate thickening of the endocardium. The lymph node was hyperplastic and contained carbon pigment.

Dog 6—On Aug 8, 1926, under ether anesthesia, two unsterile number 2 bullets and five shot were inserted in the right femoral vein of a large adult male hound. Three ribs were then resected and the heart was incised and sutured by the technic of Cutler and Beck. The dog died fifteen minutes later from collapse of the lungs. In dogs 6 and 7 an effort was made to keep the lungs expanded by positive pressure by means of a bellows and a tube inserted in the trachea. This proved unsatisfactory, and the lungs collapsed.

At necropsy the bullets and shot were found in the external iliac vein. The heart and lungs were normal.

Dog 7—On Aug 8, 1926, under ether anesthesia, one unsterile number 1 bullet and three shot were inserted in the right femoral vein of a medium sized adult female hound. A thoracostomy was done and the heart was incised and sutured as in experiment 6. The dog died twenty-five minutes later from collapse of the lungs.

At necropsy the bullets and shot were found in the external iliac vein and inferior vena cava. The heart and lungs were negative.

Dog 8—On October 4, 1926, under ether anesthesia, two unsterile nails and four shot were inserted in the left femoral vein of a small young female hound. No immediate symptoms were observed.

On October 12, the dog had no appetite, was gradually losing weight and appeared sick.

On October 15, the dog had a slight secondary bleeding from the femoral incision.

On October 16, twelve days after operation, the dog died.

Necropsy showed the dog to be emaciated. Two shot were found in the lower lobe of the left lung. The lungs were otherwise normal. Two shot were embedded in the endocardium near the apex of the right ventricle. The heart otherwise appeared normal. The abdominal viscera were negative.

Microscopic examination of sections taken near the shot in the wall of the right ventricle showed considerable thickening of the endocardium with acute inflammation of the adjoining myocardium. The wall of the right ventricle showed cloudy swelling and occasional round cells.

Dog 9—On Oct. 4, 1926, under ether anesthesia one unsterile number 4 bullet, five unsterile shot and two unsterile nails were inserted in the left femoral vein of a large adult female hound. In the suturing of the incision the femoral artery was punctured and bled freely. This was controlled by ligation of the artery. The dog reacted well immediately after the operation and apparently had no ill effects from the double ligation of the left femoral artery and vein.

On October 12 the dog did not have any appetite and was losing weight.

On October 15, the dog continued to refuse food and was rapidly becoming emaciated.

On October 17, thirteen days after operation, the dog died.

At necropsy the right pleural cavity contained several ounces of pus. An abscess about 3 cm. in diameter in the lower right middle lobe communicated with the pleural cavity. One bullet, five shot and two nails were found in the lungs. One shot was in the lower right lobe; the remaining foreign bodies were in the left lung. No bullets or shot were found in the lobe containing the abscess. The heart and abdominal viscera were negative.

Microscopic examination of sections from the lobes containing the bullets and shot showed areas resembling the gray hepatization stage of pneumonia. The margins of the abscess showed typical acute inflammation with some walling off of the abscess. Sections of the heart showed cloudy swelling but no inflammatory areas.

Dog 10—On Oct. 19, 1926, under ether anesthesia one unsterile number 1 bullet, three unsterile nails and one unsterile shot were inserted in the right femoral vein of a medium sized adult male bulldog. No immediate symptoms were observed.

On October 27 the dog appeared listless and had no appetite.

On October 29 the dog was becoming emaciated and used its left foreleg with difficulty. There was a swelling apparently in abscess near the second joint.

On October 31, twelve days after operation, the dog died.

Necropsy showed the dog to be emaciated. An abscess in the left foreleg containing about 2 ounces (60.5 cm.) of pus was opened, and two nails and one bullet were found in the wall of the abscess at a bifurcation of the brachial artery. One nail and one shot failed to leave the femoral vein owing to faulty insertion. Careful examination of the lungs and heart failed to show the point of entrance of the foreign bodies to the arterial side of the circulation. Anteriorly close to the 1 cm. in diameter were found in both ventricles of the heart.

Microscopic examination of sections showed diffuse round cell infiltration and scattered hemorrhagic areas throughout the lungs. Definite pneumonia was not made out. Sections from the heart showed slight leukocytic infiltration and several round cells with slightly thickened cytoplasm. A small area of the wall of the right ventricle showed a small hole, the size of a pin, with an irregular blackish stain on the surface.

Dog 11—On Oct 25, 1926, under ether anesthesia, one unsterile number 1 bullet and two unsterile shot were inserted in the right femoral vein of a medium sized adult female mongrel. No immediate symptoms were observed.

On November 3, under ether anesthesia, two unsterile number 2 bullets and eleven unsterile shot were inserted in the right femoral vein. No immediate symptoms were noted.

On December 20, roentgen-ray examination showed three bullets and nine shot in the left lung, and four shot in the right lung.

On December 21, the dog was killed.

Necropsy showed the dog to be well nourished. Ten bullets and shot were found in the left lower lobe, two bullets and shot in the left middle lobe, three shot in the right lower middle lobe and one shot in the right lower lobe. Macroscopic changes could not be noted in the heart or lungs. The abdominal viscera were negative.

Dog 12—On Nov 1, 1926, under ether anesthesia, four sterile nail fragments were inserted in right femoral vein of a medium sized adult male mongrel. No immediate symptoms were noted.

On November 8, under ether anesthesia, four sterile nail fragments were inserted in the left femoral vein. No immediate symptoms were observed.

On November 22, the dog died from an over administration of anesthetic prior to operation.

Necropsy showed the dog to be well nourished. Three nails were found in the right lung, and four nails in the lower lobe of the left lung. The lungs and heart macroscopically appeared normal. The abdominal viscera were negative. One nail failed to leave the femoral vein owing to faulty insertion.

Microscopic examination of sections of the lungs showed diffuse round cell infiltration with areas of marked congestion. There was slight pleural thickening and increased fibrous tissue throughout the lungs.

Dog 13—On Nov 12, 1926, under ether anesthesia, five sterile nail fragments were inserted in left femoral vein of a medium sized young female collie. No immediate symptoms were noted.

On November 21, the dog had slight secondary bleeding from the femoral incision, otherwise it appeared well.

On November 22, ten days after the operation, the dog was found dead. Death was thought to have resulted from a fight with another dog, as there had been little bleeding from the femoral incision and the dog had sufficiently recovered to permit its running at large with other dogs.

Necropsy showed the dog to be fairly well nourished, and apparently not anemic. Four nails were found in the lungs, two were together in the left lower lobe and the remaining two were in the right lung. One nail remained in the femoral vein owing to faulty insertion. The lungs appeared normal. Two small ante-mortem clots were found in the right ventricle of the heart. The abdominal viscera were negative.

Dog 14—On Dec 16, 1926, under ether anesthesia, nine sterile nails and nail fragments were inserted in the left femoral vein of a small young female airedale. No immediate symptoms were noted.

On December 20, roentgen-ray examination showed the nails in the region of the hilum of the lungs.

On December 21, the dog was killed.

Necropsy showed the dog to be well nourished. Three nails were found in the lower middle lobe and the lower lobe of the right lung. The heart was opened.

and the remaining nails were found in the pulmonary artery, with the exception of one nail fragment in the right ventricle. This had evidently fallen back into the heart owing to handling of the specimen after death, as roentgenograms made before death showed that all of the foreign bodies had passed through the heart and were in the pulmonary artery or lungs. The heart and lungs did not show any gross clumps. The abdominal viscera were negative.

COMMENT

Fourteen dogs were operated on and ninety-three foreign bodies were inserted. Of these, sixteen did not reach the general venous circulation owing to faulty technique. Eleven bullets were found in the common iliac veins or in the inferior vena cava of two dogs which died in the course of secondary unrelated operations on the thorax within thirty minutes after insertion of the bullets.

Of the remaining twelve dogs only three died as a result of the foreign bodies, and these were in the second series in which unsterilized bullets and nails were inserted into the veins. Sixty-seven objects migrated to the heart, but only three were found in the heart at autopsy. The remaining sixty-four bodies were carried through the pulmonary valves into the pulmonary artery and lungs. Roentgen-ray examinations showed these foreign bodies to be in the lungs, and this was verified at necropsy. Every foreign body which reached the junction of the iliac veins was carried upward through the inferior vena cava by the current of blood. The two dogs killed soon after the insertion of the bullets demonstrated that this migration was not an immediate thing, but probably took several hours, or perhaps even days, and may not have occurred until the dogs had recovered from the effects of the operation and were again active. This increased activity probably gave the necessary stimulus to the venous circulation to carry the heavier bodies toward the heart.

In no instance were any immediate symptoms noted which could not be explained by the anesthesia used during the operation. Two dogs had slight secondary bleeding from the femoral incisions. This apparently was due to injury to the femoral artery at the time of operation.

The lung tissue in the majority of cases showed but little macroscopic change despite the occlusion of the larger branches of the pulmonary artery by the bullets and nails. A localized dry fibrinous pleurisy was noted in one case (dog 4) in which two sterile bullets were inserted, and an abscess of the lung terminating with empyema developed following the introduction of eight unsterile nail fragments, causing death thirteen days after operation (dog 9). The results were not typical and occurred only in these two cases. It is interesting to note that the abscess of the lung developed in a lobe which did not contain any foreign bodies.

The microscopic observations were more uniform. All sections of the portions of the lungs containing foreign bodies showed pathologic changes, varying from moderate congestion with round cell infiltration to a picture simulating the gray hepatization stage of pneumonia. This probably represented the later stages of an infarct of the lung. An increase in fibrous tissue with slight thickening of the pleura was a fairly constant observation.

In the second fatal case (dog 10) two nails and one bullet passed through the heart or lungs into the arterial side of the circulation and lodged at the bifurcation of the brachial artery in the left front leg, where they caused a large abscess with death twelve days after operation.



Fig 2—Dog 8, heart containing two shot (indicated by arrows) in right ventricle, the dog died twelve days after insertion of four unsterile shot and two unsterile nails in the left femoral vein, two shot were found in the lungs and the remaining two near the apex of the right ventricle, the nails failed to leave the point of insertion owing to faulty insertion.

Careful gross examination of the heart and lungs failed to indicate the point where these foreign bodies gained access to the arterial side, the lungs did not show any macroscopic lesion, and the heart contained only two moderately large antemortem clots. Microscopic sections of this lung demonstrated several hemorrhagic areas and regions of moderate round cell infiltration. The wall of the heart showed slight cloudy swelling, occasional round cells and thickening of the endocardium, with a small ulcerated area in the wall of the right ventricle and localized acute inflammation and an antemortem blood clot at the margin of the ulcer.

In the third fatal case (dog 8) two shot were found to have lodged at the base of the chordae tendinae near the apex of the right ventricle, death having occurred twelve days after the operation (fig 2). No

other cause of death could be found. Microscopic examination of the heart near the site of the bullets showed cloudy swelling and occasional round cells. There was considerable thickening of the endocardium with acute inflammation of the adjoining myocardium. The only other case in which a foreign body remained in the heart did not terminate fatally (dog 5). Ten days after the last insertion of foreign objects this dog was killed, and the shot was found at necropsy at the apex of the right ventricle (fig. 3). It had not caused any symptoms and was almost embedded in the endocardium near the base of the chordae tendinae. Three bullets of .177 caliber had also been inserted into this dog. These were found in the lungs.



Fig. 3—Dog 5, heart containing one shot (indicated by arrow) in right ventricle. At first operation two bullets were inserted in the right femoral vein, sixteen days later one bullet and seven shot were inserted in the left femoral vein, the dog was killed five days after the second operation. At necropsy the bullets were found in the lungs, six shot remained at the point of insertion in the femoral vein, the seventh shot migrated to the heart and was found near the apex of the right ventricle.

In no instance was a foreign body found in the right auricle, or in the left side of the heart. No relationship apparently existed between the veins (jugular or femoral) in which the bodies were inserted, and their ultimate lodging place. The foreign bodies carried to the lungs by the blood stream were not symmetrically distributed throughout the lung tissue, but were most frequently found clumped together in two or three branches of the pulmonary artery (figs. 4 and 5). The majority of the objects lodged in the lower lobes of the left lung. This is probably due to a larger lumen and greater blood flow through the

branches of the pulmonary artery supplying the left lung, which in the dog has only three lobes as compared with the right lung which has four lobes

With the exception of the two fatal cases with abscess formation there apparently was little reaction around the bullets or nails in the lungs



Fig 4—Dog 11, lower lobe of left lung showing a branch of the pulmonary artery containing four shot and two bullets, thirteen shot and three bullets were introduced into the femoral veins in the course of two operations, the dog was in excellent health when killed eighteen days after the last operation, the remaining bullets and shot were scattered throughout both lungs

The majority of the foreign bodies were of steel, but no difference could be noted between these and those of lead. In no instance were thrombi found in the pulmonary artery, and only three small antemortem clots were noted in the right ventricle

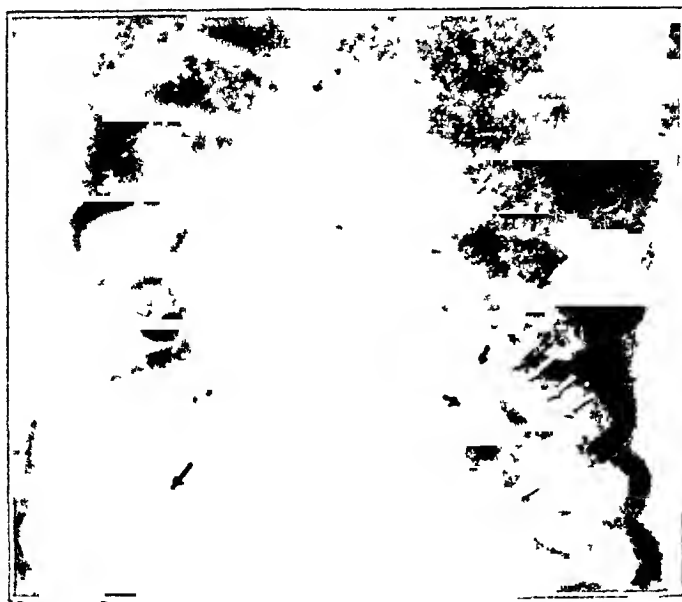


Fig 5—Dog 11 three bullets and thirteen shot scattered throughout both lungs—only four shot were found in the right lung—the remaining twelve bullets and shot were contained in the left lung



Fig 6—Dog 1, one number 1 bullet in lower lobe of left lung

Five nails in the pulmonary artery and a sixth nail which had evidently fallen back into the right ventricle, owing to handling of the specimen after death, were found in dog 14 (figs 8 and 9). This failure to reach the lungs was probably due to the length of several of the nails, which were unable to negotiate the curve of the pulmonary artery, as three shorter nails were found in the lungs. The blood flowed around these bodies without obstruction and ill effects were not noted. One nail in this group extended halfway through a fibrous band resembling a rudimentary valve situated just above the pulmonary valves. It had doubtless passed by this valvelike septum during systole and was

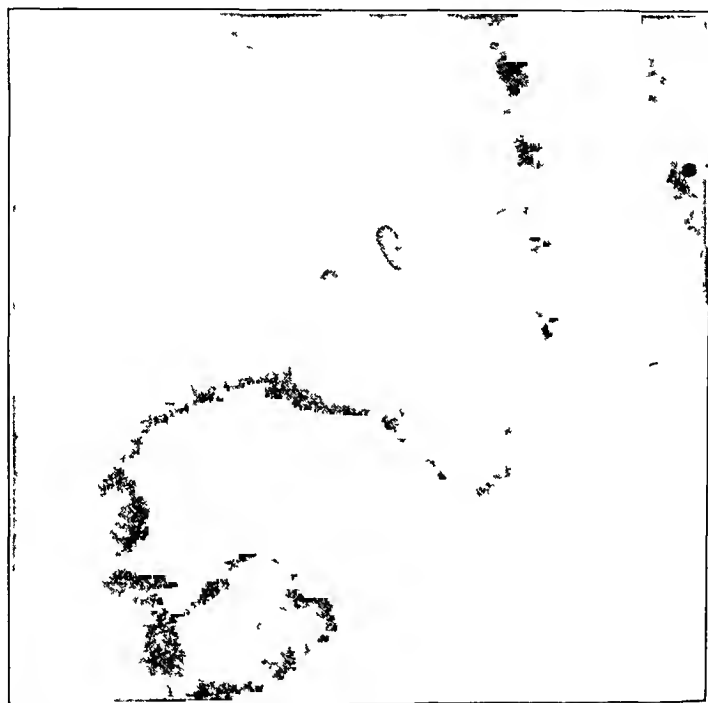


Fig 7—Dog 3, one number 1 bullet in lower lobe of left lung, the small shot are in the subcutaneous tissues and are evidently the result of the dog having been shot prior to the experiments

then caught in a backflow, gradually puncturing the fibrous septum. These nails which had passed through the heart varied from 18 to 32 mm in length. With the exception of one small antemortem clot around the nail held in the rudimentary valve, the heart and the pulmonary artery did not show any lesion resulting from the passage of these irregularly shaped objects, and the dog appeared in good health.

The recent work of Cutler¹⁰ and his associates in surgery of the heart has opened a new field, and serves as a stimulus to further studies

10 Cutler, E. C., Levine, S. A., and Beck, C. S. The Surgical Treatment of Mitral Stenosis. Experimental and Clinical Studies, *Arch Surg* 9:689 (Nov) 1924.

in this phase of surgery. Beck¹¹ described a technique of suture in heart wounds which would lend itself admirably to the removal of foreign bodies within the cavities of the heart. He favors a median sternotomy or a left intercostochondrial thoracotomy. The former gives a better exposure of the right ventricle. The pericardium is opened and a suture to steady the heart is placed in the apex of the heart. After the foreign body is palpated in the cavity of the heart two parallel control sutures taking a deep bite in the muscle of the heart wall are placed opposite the site of the foreign body within the heart. A longitudinal incision is

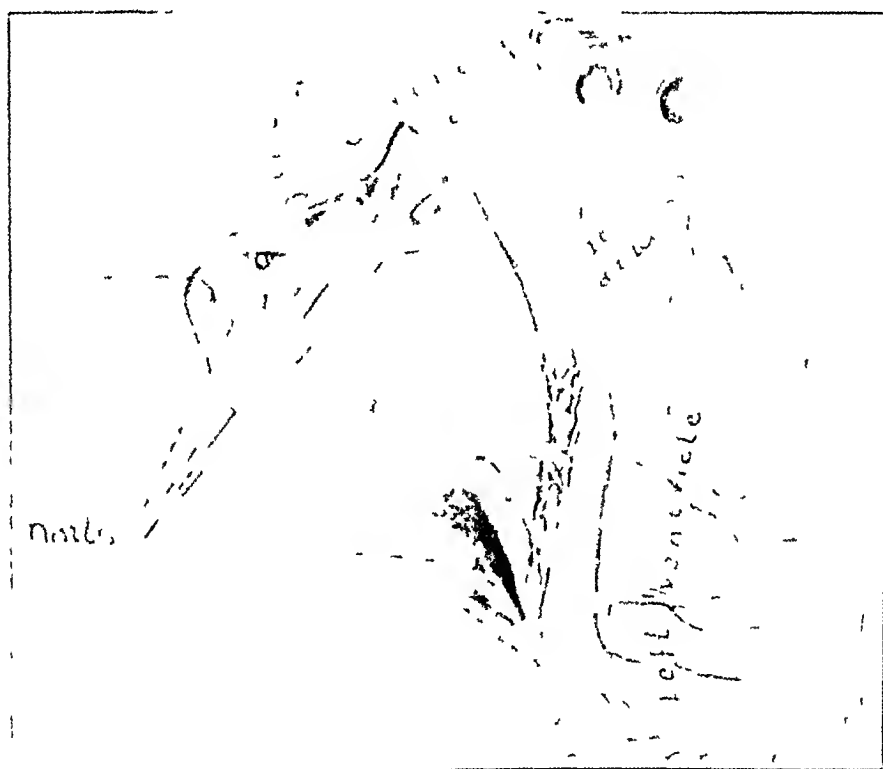


Fig. 8.—Dog 14, nail in pulmonary artery and right ventricle, dog was killed five days after insertion of two nails in the left femoral vein, roentgenograms before death showed three nails in the right lung and the remaining six in the pulmonary artery, when the heart was opened at necropsy one nail was found in the right ventricle, evidently having fallen back due to manipulation after death, one nail is shown caught in a fibrous band simulating a rudimentary valve.

made in the tissue suspended between the control sutures, through which the foreign body is removed. The control sutures are then crossed and held under gentle traction by an assistant, thus approximating the edges of the incision while permanent sutures are placed and a neat closure is obtained.

¹¹ Beck, C. S.: Wounds of the Heart. The Technique of Suture, Arch. Surg. 13: 205 (Aug.) 1926.

SUMMARY

The following types of foreign bodies have been discussed Bullets inserted in venous circulation, 22, shot inserted in venous circulation, 43, nails inserted in venous circulation, 29, total number of foreign bodies, 94

Sixteen of the foreign bodies failed to leave the femoral vein owing to faulty insertion

Eleven were found in the external iliac vein and in the inferior vena cava of two dogs killed thirty minutes after insertion, in the course of a second unrelated operation



FIG 9—Dog 14, nine nails and nail fragments, three nails were in the right lung, the remaining nails were within the pulmonary artery

Sixty-seven foreign bodies migrated to the heart, and of this number

Three (4.5 per cent) remained in the heart The three animals were shot and in each the foreign body lodged near the apex of the right ventricle Death resulted in one case

Six (9.0 per cent) remained in the pulmonary artery, their length apparently preventing them from passing into the lungs

Fifty-five (82 per cent) passed into branches of the pulmonary artery and lodged in the lungs Death resulted from abscess in one dog

Three (4.5 per cent) passed through the heart or lungs of one dog, reached the arterial circulation and lodged at the bifurcation of the brachial artery in the foreleg, causing a large abscess, and resulted in death.

The total number of dogs operated on was 14.

Two were killed immediately following operation.

Three (25 per cent) died as a result of the insertion of bullets or nails into the veins.

Twelve sterile bullets and shot were inserted in the veins of three dogs. There were no deaths.

Twenty-two sterile nails were inserted in three dogs. There were no deaths.

Forty-five unsterile bullets and shot were inserted in six dogs with death in one instance (16.6 per cent mortality). Two shot were found in the right ventricle in the fatal case.

Five unsterile nails were inserted in two dogs. Both dogs died (100 per cent mortality). One dog had an abscess of the left lung with empyema, and the other had an abscess in the left foreleg.

NOTE.—The discrepancy between the total number of foreign bodies introduced, and the number enumerated in these four groups is due to dogs 3 and 5 having both sterile and unsterile bullets and shot inserted, and dogs 9 and 10 having both bullets and nails inserted. In order to avoid this overlapping, in dogs 3 and 5 only the unsterile bullets and shot were considered, and in dogs 9 and 10 only the nails were tabulated in this summary.

CONCLUSIONS

- 1 Foreign metallic bodies within the lumen of a normal vein of a dog are carried by the blood stream toward the heart. This migration may take hours, or days, but eventually these wandering bodies reach the heart, irrespective of the position of the dog and the effects of gravity.

- 2 The majority of these objects do not remain in the heart, but are pumped into the pulmonary artery and lodge in the lungs, where they produce infarcts with apparently little disturbance to the pulmonary circulation.

- 3 The presence of these foreign bodies within the lungs appear to cause little discomfort. Abscess of the lung occurred only once in this series, and this abscess did not arise in a lobe containing foreign bodies. This would indicate that operative procedures in such cases would not be advisable in the absence of marked symptoms of pulmonary involvement.

- 4 Sterilized foreign bodies in the venous circulation do little damage to the heart or lungs, and unsterilized objects which are smooth and

symmetrical rarely cause infection. Unsterilized, irregularly shaped bodies, as nails or fragments of nails, are most dangerous and give rise to abscesses.

5 The smaller, more symmetrical and lighter objects in the venous circulation tend to remain in the heart, while the larger, more irregular and heavier bodies are carried into the lungs. Foreign bodies that remain in the heart appear to lodge near the apex of the right ventricle at the base of the chordae tendinae. This is the most accessible portion of the heart in both dog and man. The recent work of Cutler¹⁰ and Beck¹¹ in intracardiac surgery provides a technic which would greatly facilitate the removal of foreign bodies from this region of the heart.

6 It is possible for objects to pass from the venous to the arterial circulation, this transition probably occurring in the lungs, without leaving any macroscopic evidence of pulmonary damage.

OPERATIONS OF NECESSITY DURING PREGNANCY^{*}

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We shall discuss here conditions amenable to surgical intervention that may complicate pregnancy, but that are not the results of it. However, certain physiologic and anatomic changes incident to pregnancy may influence certain associated lesions and add to the gravity of the surgical risk. Examples of this are (1) the rapidity with which certain types of tumors of the breast and uterus grow as a result of the increased blood supply incident to pregnancy, (2) changes in the relative position of the pelvic organs and some of the abdominal viscera caused by the enlarging uterus with disturbance of quiescent lesions, and (3) the probability that the retardation in the filling and emptying of the gallbladder during pregnancy and the increased cholesterol content of the blood are factors in the formation of gallstones during pregnancy and even exacerbation of quiescent cholecystitis.

In the examination of women in the child-bearing age for conditions of surgical importance one must always be alert to the possibility of pregnancy. In a review of the histories of a large group of women in the child-bearing age who presented themselves at the Mayo Clinic because of surgical lesions, it was found that approximately 2 per cent were pregnant. Certain preexisting lesions are likely to grow worse during pregnancy or, because of their situation, cause interference with the normal progress of pregnancy and labor. In determining the method of treatment to be advised in these cases, the following questions must be considered:

Is it reasonably certain that a lesion exists? Is a surgical operation the best treatment for the lesion? Will the general condition of the patient permit of operation? Does the severity of the trouble justify operation during pregnancy, and, if so, when is the best time to operate? What is the relative risk to mother and to child?

These questions must be considered from the standpoints of the type of condition and of the individual case. The surgical conditions are naturally grouped into those that may and those that may not be influ-

^{*} From the Section on Obstetrics, Mayo Clinic.

^{*} Read before the Pacific Northwest Medical Association, Boise, Idaho, June, 1927.

enced by pregnancy. The first group is by far the larger and the more important, as it includes intra-abdominal and pelvic lesions as well as such extra-abdominal lesions as tumor of the breast, certain types of goiter, varicose veins and hemorrhoids. The second group may be said to include surgical lesions of the head, neck, chest and extremities.

The histories of 370 women on whom it was necessary to operate during pregnancy were reviewed from Jan 1, 1917, to Jan 1, 1927. Before the results of this review are presented, it should be said that during this period an approximately equal number of pregnant women who presented themselves with surgical lesions did not come to operation. A third group, on whom operations were performed, is not included because subsequent data to confirm the diagnosis of pregnancy were lacking (table 1).

TABLE 1—*Operations of Necessity During Pregnancy*

Operation	Patients	Miscarriages	Maternal Death
Appendectomy	122	2	2
Cholecystectomy with appendectomy	47	2	
Miscellaneous on the gallbladder	27	1*	2
Partial thyroidectomy (exophthalmic goiter and adenomatous goiter with hyperthyroidism)	42†	2	
Partial thyroidectomy (adenomatous goiter without hyperthyroidism)	13†	1	
Myomectomy	13	3	
On the ovary	20	3	
On the breast	16	1	
On the kidney	14	1	
On the stomach	4		
Miscellaneous (intra abdominal)	14		
Miscellaneous (extra-abdominal)	38	1	
Total	370	17 (4.5 per cent)	4 (1.08 per cent)

* Miscarriage with death of mother from postoperative hemorrhage and obstructive jaundice.

† These data were collected between Jan 1, 1916, and Jan 1, 1926.

The list of operations performed will not be given in detail, and only the lesions most frequently encountered and those of unusual interest will be discussed. In a number of instances, more than one lesion was treated surgically at the time of operation.

COMPLICATING LESIONS

Appendicitis—Appendicitis is a fairly common complication of pregnancy. Approximately 2 per cent of the women who presented themselves with symptoms of appendicitis were pregnant. Paddock¹ found the incidence to be 2.5 per cent. Attacks of acute appendicitis do not occur more frequently in pregnant than in nonpregnant women but the risk of serious complications is greater in the former and this

1 Paddock, C. E. Pregnancy Complicated by Appendicitis, *Am J Obst* 68:401, 1913.

risk increases progressively. The danger of operation after the fifth month is also greater. Attacks due to chronic appendicitis are more likely to recur during pregnancy, possibly because the normal regularity of the bowels is disturbed or because the cecum has been displaced by the enlarging uterus. Since the symptoms of pyelonephritis of pregnancy may simulate the symptoms of acute appendicitis, it is always necessary to rule out the former before definite diagnosis of appendicitis is made. This usually can be done by the examination of a catheterized specimen of urine from the bladder or, if necessary, from the ureter, to detect the presence or absence of pus.

Appendectomy is indicated following one or more definite attacks of appendicitis during pregnancy. One hundred and twenty-two patients were operated on for appendicitis. Two patients died, one following operation for acute appendicitis during the sixth month, and one following operation for ruptured appendix in the seventh month of pregnancy. The only miscarriages which occurred in this group were coincident with these two deaths.

Disease of the Gallbladder—The gallbladder may become diseased during pregnancy. In 1911, W. J. Mayo² stated that 90 per cent of women who have gallstones and who have borne children date the onset of symptoms from a particular pregnancy.

The first symptoms may occur during the later months of pregnancy and are rarely severe enough to require surgical intervention. Frequently, however, preexisting cholecystitis will undergo exacerbation during the early months of pregnancy, and operation may be necessary. The danger of a waiting policy is much less than that in the case of appendicitis. However, when the attacks are frequent and severe or are accompanied by evidence of acute inflammation of the gallbladder, operation should be considered.

Seventy-four operations were performed on the gallbladder and ducts, and in forty-seven of these the appendix also was removed. There were two miscarriages but no maternal deaths. In four cases, the common duct was drained at the time of cholecystectomy. One of these patients died from hemorrhage complicating obstructing jaundice, and miscarriage occurred coincident with her death. There was one maternal death following choledochotomy alone (table 2).

Pelvic Tumors—It is often difficult to make a diagnosis of pelvic tumor complicating pregnancy or to distinguish the condition from intra-uterine or ectopic pregnancy. Even when the diagnosis of pregnancy and tumor has been made, it is not always easy to determine the type of the tumor. The differential diagnosis is important, as the treat-

² Mayo, W. J. Innocent Gall-Stones a Myth, J. A. M. A. 56: 1021 (April 8) 1911.

ment may vary with the nature of the tumor. In most cases of fibromyoma of the uterus the patient will go through pregnancy and confinement without untoward symptoms. Certain fibromyomas are so situated that they will obstruct the birth canal, others may undergo degeneration and still others may cause hemorrhage and abortion. When the tumor is situated low in the pelvis so that it is likely to cause dystocia its removal may be necessary during pregnancy; otherwise cesarean section at term would have to be performed. Many myomas cause pain and tenderness during pregnancy; the patients are usually treated expectantly as most of them can be carried to term. Sometimes on account of the marked pain and tenderness and evidence of peritoneal irritation enucleation of the myoma is found necessary during pregnancy. In the case of uterine myomas in which the patient gives

TABLE 2—Operations on Gallbladder and Ducts During Pregnancy

Operation	Patients	Miscarriages	Maternal Death
Cholecystectomy	22	1*	
Cholecystectomy and appendectomy	1	2	
Cholecystectomy and choledochotomy	4	1†	1
Choledochotomy	1		1
Total	74	4 (5.4 per cent)	2 (2.7 per cent)

* Miscarriage twenty-third day after operation.

† Maternal death of mother from peritonitis.

TABLE 3—Myomectomy During Pregnancy

Operation	Patients	Miscarriages
Myomectomy	8	1
Myomectomy and appendectomy	4	2
Myomectomy and excision of Bartholin cyst	1	
Total	13	3 (23 per cent)

a history of previous miscarriages apparently due to the tumor or in which symptoms of threatened miscarriage are being produced by the tumor myomectomy may be employed as a conservative measure. In 1920 W. J. Mayo³ reported having performed myomectomy nineteen times during pregnancy. Five of the patients showed signs of impending miscarriage prior to operation and in three the miscarriage was averted by the operation.

Myomectomy was performed in thirteen cases of our series. These include some cases previously reported and several others. There were three miscarriages and no maternal deaths (table 3).

³ Mayo W. J. Conservation of the Menstrual Function. J. A. M. A. 74: 1685 (June 19) 1920.

Ovarian cysts are likely to cause more difficulty than myomas. Tumors of the ovary which usually lie low in the pelvis cause dystocia and there is danger that they may rupture during labor. It has generally been conceded that if these tumors attain considerable size they should be removed during pregnancy. The decision with regard to this must be guided, however, and will depend mainly on the site of the tumor and on the period of gestation. In Barrett's⁴ series, in which expectant treatment of the tumor was carried out, the maternal mortality was 18.4 per cent, as against 2 per cent in patients treated surgically.

Nineteen operations were performed for cystic tumors of the ovary during pregnancy. In six of these cases salpingectomy was also performed and in eleven cases the appendix was removed secondarily. In all but one case oophorectomy was performed. There were three miscarriages and no maternal deaths (table 4).

It has been thought that exophthalmic goiter and adenomatous goiter with hyperthyroidism were incompatible with the continuation of

TABLE 4—*Operations on the Ovary During Pregnancy*

Operation	Patients	Miscarriages
Oophorectomy (single)	1	
Salpingo oophorectomy (single)	6	2
Puncture of ovarian cyst	1	
Oophorectomy with appendectomy	11	1
Total	19	3 (15 per cent)

pregnancy. In a review of cases of pregnancy complicating goiter published in 1925 it was found that since 1916 pregnancy had been observed in the Mayo Clinic in thirty-two patients having exophthalmic goiter and in ten having adenomatous goiter with hyperthyroidism.⁵ Either ligation or partial thyroidectomy or both were successfully performed in thirty-four cases, and since the introduction of iodine as an aid in the treatment of exophthalmic goiter, ligations have been found unnecessary as a preliminary procedure to partial thyroidectomy. When advisable for the control of exophthalmic goiter or adenomatous goiter with hyperthyroidism, partial thyroidectomy, with proper precautions, has been performed on the pregnant woman with reasonable safety to both mother and child. Maternal death did not occur. Spontaneous abortion occurred twice and premature labor twice, apparently due largely to

4 Barrett, C. W. Ovarian Tumors Complicating Pregnancy, Delivery, and the Puerperium, *Surg. Gynec. Obst.* 16: 28, 1913.

5 Mussey, R. D., Plummer, W. A., and Boothby, W. M. Pregnancy Complicating Exophthalmic Goiter and Adenomatous Goiter with Hyperthyroidism, *J. A. M. A.* 87: 1009 (Sept. 25) 1926.

other complications. In certain cases the thyroid gland enlarges during pregnancy. In most cases this is due to diffuse colloid goiter, and in some cases adenoma may be present. In fact, it is probable that a diffuse colloid goiter in a woman more than 25 years of age may contain nonpalpable adenoma. The necessity for the removal of adenomatous goiter without hyperthyroidism rarely arises during preg-

TABLE 5—*Exophthalmic Goiter and Pregnancy**

Treatment Prior to Use of Iodine	Cases	Miscarriages
Rest and observation	2	1
Ligation of superior thyroid artery	8	1
Ligation followed by partial thyroidectomy	4	
Thyroidectomy (alone)	6	
Treatment After Use of Iodine		
Iodine	5	
Iodine followed by partial thyroidectomy	7	

* These data were collected between Jan 1 1916 and Jan 21, 1926

TABLE 6—*Adenomatous Goiter Complicating Pregnancy**

Treatment in Patients with Hyperthyroidism	Cases	Miscarriages
Rest and observation	1	
Ligation	2	
Ligation and thyroidectomy	1	
Thyroidectomy	4	
Iodine thyroidectomy	1	
Quinine and injection of urea	1	
Treatment in Patients Without Hyperthyroidism		
Partial thyroidectomy	13	1

* These data were collected between Jan 1, 1916, and Jan 1, 1926

TABLE 7—*Operations on the Kidney and Ureter During Pregnancy*

Operation		Patients	Miscarriages
Nephrectomy			
Tuberculosis of kidney	5		
Pyelonephrosis	2	7	1
Ureteronephrectomy			
Stone in ureter	1		
Hydronephrosis infection	1	2	
Pelviolithotomy			
Stone in left kidney	2	2	
Ureterolithotomy			
Stone in right ureter	3	3	
Total	14	14	1 (7.14 per cent)

nancy, but in some instances the size or situation of the tumor causes pressure symptoms which demand partial thyroidectomy (tables 5 and 6)

Operation is performed on the kidney during pregnancy when the lesion is such that the life or future health of the mother would be jeopardized by delay. In this series there were fourteen operations on the kidney, including nine nephrectomies. There was one miscarriage and no maternal death (table 7)

A miscellaneous group of operations was performed, including splenectomy for hemolytic jaundice in one case, resection of the stomach for carcinoma in one case, gastro-enterostomy in two cases and the closure of a gastro-enteric stoma in one case. Posterior resection of the rectum for carcinoma was performed (four and a half months' pregnancy) following a preliminary colostomy, and a living child was delivered by cesarean section at term. Five other rectal operations were performed, including hemorrhoidectomy, repair of prolapsed rectum and excision of anal fissure. There was no maternal death or miscarriage in this group. Sixteen operations were performed on the breast, including radical amputation for carcinoma in five cases, simple amputation in two cases and excision of tumor in eight cases. There was one miscarriage and no maternal death. The remaining miscellaneous operations included herniotomies, explorations, elevation of the pregnant uterus impacted in the pelvis, biopsy from the cervix for suspected carcinoma and the removal of a bleeding cervical polyp.

COMMENT

Operations of necessity were performed on somewhat less than half of the pregnant women presenting themselves with surgical lesions. The treatment of the remainder of the group depended on the nature of the lesion and on the period of gestation. Patients with gallstone colic, patients with a history of appendiceal attacks and patients with uterine fibromyomas should be carefully observed.

If surgical intervention is found necessary during pregnancy, it should not cause more than ordinary concern. The mortality rate is not greater than that following similar operations on nonpregnant women. The number of miscarriages is not appreciably greater as a result of the operative procedure than the normal expectancy of miscarriages during pregnancy. The time of election for operations is in the first five months, although extra-abdominal operations can be performed at almost any period of gestation. Varo⁶ has emphasized the point that, if possible, pelvic operations should not be performed at a time when the menses would have occurred were the patient not pregnant. Intra-abdominal operation should not be performed after the sixth month if it can possibly be avoided.

Briefly stated, the postoperative treatment consists of the hypodermic injection of from 1/6 to 1/4 gram (0.11 to 0.16 Gm.) of morphine every four hours for the first two or three days, the amount and frequency of the dosage being gradually diminished, according to the condition of the patient. The patient is not given a laxative by mouth until the

⁶ Varo, B. V. The Prevention of Abortion After Operations on Pregnancy, *Zentralbl. f. Gynak.* 50:1964, 1925.

fifth or sixth day and then only a mild one. Retention enemas of about 2 ounces (62 Gm) of warm sweet oil may be given on the third or fourth night, to be followed the next morning by an 8 ounce (248 Gm) simple enema. The patient is given the usual postoperative diet.

SUMMARY

Operations should be deferred until after confinement, if possible. Any necessary operation can be performed prior to the fifth month of gestation without undue risk to mother and child.

Operation for uterine myoma is rarely necessary during pregnancy. The removal of large cysts of the ovary is less dangerous to the mother than expectant treatment.

Gastrectomy, splenectomy, nephrectomy and resection of the rectum for carcinoma may be performed without undue risk during pregnancy.

TREATMENT OF INFECTION

GENERAL PRINCIPLES UNDERLYING TREATMENT FROM THE
SURGICAL STANDPOINT AND THERAPEUTIC INDICATIONS
TO BE DRAWN THEREFROM*

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In a previous communication¹ the general mechanism of acute bacterial infection of the body was extensively discussed. Infection exhibits itself (1) as a more or less local lesion with general manifestations derived from the absorption of toxins from bacteria, or (2) as a generally similar entity with which a bacteremia or general blood infection is associated. In this communication I will discuss the general principles underlying the treatment of acute bacterial infection from the surgical standpoint, and will pay especial attention to the group of cases in which bacteremia or general blood infection is demonstrable.

CLINICAL CLASSIFICATIONS

Blood cultivations of the peripheral blood can be employed in cases of acute infection for the following purposes: (a) in appropriate cases as an additional means of differential diagnosis, (b) as a means by which the severity of the infection can be gaged, (c) as a help in estimating the prognosis and (d) as criteria on which to base the primary or further operative treatment.

A relative quantitative estimation of the magnitude of the infection can be established according to the number of colonies of bacteria which appear on the plate (plate culture method) in proportion to the amount of blood used to inoculate the culture medium in the plate, thus one or five colonies of bacteria per cubic centimeter of blood as compared with 100 or with an uncountable number of colonies of bacteria per cubic centimeter of blood. This is a rough method and is not strictly accurate, but for practical purposes the inaccuracy is inconsequential.

Clinical Grouping According to Extent of Bacteremia—In practice, the presence or absence of bacteremia or general blood infection and its relative magnitude yield the following clinical groupings, and the correct interpretation of the bacteremia in its relation to the clinical manifestations yields certain therapeutic indications.

A Treatment for the bacteremia or general infection is many times not called for, as commonly the natural protective agencies of the body

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1 Wilensky, Abraham O. The Mechanism of Bacterial Infection, Arch Surg 13 228 (Aug) 1926.

are able to destroy the bacteria and their effects as fast as the organisms and their toxins find their way into the circulation. Many times, also, as pointed out on previous occasions the bacteriemia which accompanied the demonstrable or undemonstrable primary focus of infection at its point of entry and which was caused by it, or which in turn fathered the development of one or more demonstrable subsidiary foci of infection, was a temporary phenomenon, and sufficient time had elapsed between its appearance and the moment of observation to allow for its spontaneous disappearance. Under these circumstances, there may be no clinical or laboratory evidences of its existence. Good prognoses should be the rule under these circumstances, and the method of treatment should be planned with regard to the local focus of infection only. A reservation should be made in one's mind, however, to cover those cases of acute infection in which, for some undefinable reason as previously explained, the thrombophlebitis begins to spread, in these cases positive blood cultures may be obtained later, and the character of the illness may change entirely for the worse.

B Blood cultures showing from one to five colonies of organisms to the cubic centimeter of blood are usually, but not always, of a mild nature, frequently show little or no evidence of their existence, are associated with symptom complexes which do not differ materially from those in similar cases in which the blood cultivations are sterile, and frequently disappear spontaneously or after operation. Good prognoses are the rule in these minor bacteriemias, and the method of treatment usually can be planned without regard to the bacteriemia.

C On the other hand blood cultures can be obtained in which the numbers of colonies are extremely large, 100 or more colonies to the cubic centimeter of blood. This always indicates a severe infection and an extremely grave prognosis. The clinical picture commonly shows an equal evidence of the severity of the infection.

This group contains those fulminating, progressive and severe forms of bacteriemia and general blood infection, the existence of which is associated clinically with a symptom complex in which a demonstrable local focus of infection is of minor and secondary consideration, and in which the bacteriemia or general blood infection is the dominating factor in the entire clinical picture. The local focus may exhibit definite signs of its presence or may be unrecognizable and undemonstrable, owing to either the paucity of its clinical manifestations or the profound intoxication produced by the general blood infection.

Any kind of local condition may be associated with such a general infection. It is to be assumed under such conditions that large numbers of viable organisms are being discharged into the blood stream from the thrombophlebitic tissue, and that the bacteria are multiplying in the

blood also, the prognosis must therefore be serious. The usual course of the condition includes a steady progression of the general blood infection until a fatality occurs.

Under these circumstances, treatment directed to the local lesion is clinically futile, and fatalities are the rule and not the exception. Even the most radical surgical procedure, such as amputation of an extremity, is of no avail clinically, and the uselessness of such a radical procedure or other procedures is usually easily recognizable by the hyperacuteness of the infection, by the extraordinary toxicity of the clinical picture and by the overwhelming rapidity with which the latter passes into one of terminal delirium, coma and death. The premise that operation on the demonstrable foci furnishes the unfortunate patient his only chance sometimes may not be refused in the presence of anxious parents and relatives, but whenever such earnest desires are acceded to, it should be unequivocally emphasized that the "chances" are practically nil. In the fulminating cases, the entire duration of the illness is often only a few days.

There are other somewhat less severe forms of acute infection in which the blood contains also large numbers of viable organisms, but in which the clinical picture does not carry with it that comparatively sudden overwhelming of the body with a profound toxemia. A somewhat more hopeful attitude can be entertained in these cases, and whenever the local conditions make it possible, the question of a radical surgical procedure should be discussed in the hope of controlling the bacteriemia or general blood infection, this includes the question of amputation in infections of the bones and joints of sufficient severity in the extremities.

D Between these two extremes are large numbers of cases in which the cultivation of the blood shows an intermediate number of colonies of bacteria. Correct judgments are more difficult in these cases. Usually an aggressive policy is indicated, and when the local foci of infection with which the bacteriemia is associated lend themselves to surgical intervention, operation should be performed with the object of removing the thrombophlebitic lesion from which the bacteriemia is derived. Thereafter watchfulness and repeated blood culture studies are necessary. A careful study of the latter permits certain deductions of therapeutic value.

In cases of this kind when a given blood culture is compared with subsequent ones taken on the same patient, decrease in the number of colonies or their disappearance undoubtedly indicates improvement when other conditions are equal, an increase in the number of colonies should always cause alarm, a prompt reconsideration of the available clinical picture and revision of all of the demonstrable foci according to rules that I shall give. Comparisons made along these lines are of extreme usefulness and importance in work at the bedside and in the operating room.

In the presence of a positive blood culture a prognosis of the ultimate outcome should not be attempted except after consideration of all the available clinical facts. While a positive blood culture is always serious, the seriousness of the possibilities is usually paralleled by the characteristics of the clinical picture. The prognosis should always be guarded. Much depends on the availability of the local focus of infection for thorough surgical removal, and on its removal before other complicating foci have appeared. Much depends also on the patient's natural recuperative powers and on the antibacterial powers of the blood serum. Instances repeatedly occur in which these powers are sufficient to overcome the demonstrable bacteremia, so that at no time, in the absence of evidence of a fulminant and overwhelming infection as previously mentioned, should a hopeless attitude be entertained.

Infections in Which Negative Blood Cultures Are Obtained—Negative (sterile) blood cultures obtained either primarily or secondarily should not always be associated in one's mind with the milder type of infection or with improvement. The contrary may be true and negative blood cultures may occur in the presence of the most profound infections. Negative blood cultures are obtained clinically as follows:

1 In most classes of cases, notably in furuncles, carbuncles, pulmonary and renal infections, infections in the cellular spaces or in the fascial planes, positive and negative blood cultivations of the peripheral blood are about equally common in the presence of an equally severe clinical picture.

2 In infection limited strictly to the lymphatic chains—both lymphatic vessels and lymphatic glands—positive blood cultures are not obtained. This rule seems to be absolute.

3 In streptococcus (erysipelas) cellulitis of the skin, positive blood cultures are not obtained. However, when such an infection begins in the mucous membrane of the nasopharynx and spreads outward on the skin of the face, forehead and scalp, positive blood cultures are rarely obtained.

4 In a large group of cases in which the path of infection, i.e., the path by which the bacteria communicate with the general circulation, lies through the portal area, positive blood cultures do not occur, this is especially true in pyelphlebitis, and when a clinical picture is obtained sufficient to make one entertain this diagnosis, the occurrence of a positive blood culture is equally sufficient to destroy the assumption.

5 In infection of gallbladder and biliary tract, positive blood cultures do not occur either before or after operation. Positive blood cultures after operations on the gallbladder or biliary tract are usually associated with a suppurative angiocholitis and, to a less extent, with thrombophlebitic lesions which are frequently undemonstrable even at postmortem and which necessarily escape the portal area. The latter may be located in the operative wound and have no relation to the liver itself. The prognosis is extremely bad, and the patients usually go on to a fatal issue.

6 Acute infections of the pancreas—the various forms of acute pancreatitis—are not associated with positive blood cultures. These can be classified as lymphangitides of the body of the pancreas.

7 Acute splenitis—infection of the spleen (this does not include acute enlargements of the spleen associated with specific diseases such as typhoid fever, etc.)—is not associated with positive blood cultures

8 In postpartum infection, negative blood cultures are obtained as a rule. Positive blood cultures occur as exceptions, frequently, but not always, these are found to be associated with a thrombophlebitis of the large veins derived from the uterus which has succeeded in spreading into the internal iliac veins and into the venous cavity. Radical operation is permissible only when such a pathologic condition is expected with a reasonable degree of certainty, and this measure will be successful in proportion to the ability to get beyond the thrombophlebitis when the radical hysterectomy is performed. Instances of this kind are relatively uncommon.

9 In mastoid disease uncomplicated with involvement of the lateral sinus, positive blood cultures are not demonstrable. Clinically, this point has come to furnish the most important single evidence for exclusion of involvement of the lateral sinus.

10 In thrombophlebitis of the cranial sinuses, other than the lateral or petrosal sinuses, sterile blood cultures are constantly obtained. Cavernous sinus thrombosis is the best example. In the presence of a primary lesion, to which the cranial (cavernous) sinus thrombosis is secondary, a positive blood culture is sometimes obtained when the primary lesion—for example, a furuncle of the nose or face—is capable of discharging living bacteria into a blood stream.

11 In empyema thoracis strictly limited within the pleural sac and without an open communication with the pulmonary parenchyma, negative blood cultures are the rule. The occurrence of a positive blood culture should be considered an indication that some complication exists from which the positive blood culture is derived.

12 In acute peritonitis, sterile blood cultures are obtained as a rule. In the variety in which there is a distinct metastatic lesion, i.e., that secondary to an acute streptococcus tonsillitis or that secondary to a lobar pneumonia, the occurrence of a positive blood culture should be referred to the primary lesion. In the variety due to the close relationship with a primary intra-abdominal lesion, i.e., that accompanying in acute appendicitis, etc., the occurrence of a positive blood culture should be referred to some other complicating lesion; these cases are rare.

13 In acute meningitis of the suppurative variety, sterile and positive blood cultures occur about equally often. The organisms demonstrable in the blood should be referred to a thrombophlebitic lesion in close relationship with the meninges and from which the meningitis is derived.

These clinical classifications can be further combined into the following broad groups without consideration of the location of the focus of infection

2 The usual rule in conservative circles is not to operate in cases of postpartum infection, as it is found clinically that in large series of cases this policy results in a larger proportion of cures. I approve of this rule, but, nevertheless, I believe that it should not be allowed to stand in the way of operation when a case occurs in which the laboratory and clinical facts approach those outlined in the text.

A The question of a positive blood culture, being intimately associated with the presence of a thrombophlebitis in which the thrombus harbors organisms actively growing on a surface in open communication with the freely circulating blood, it follows that sterile blood cultures of the peripheral blood will be obtained under the following conditions

(a) When the primary focus of infection at the portal of entry on a surface of the body (skin or mucous membrane) does not contain a thrombophlebitis. In these instances the focus of infection is limited to cellular tissue or spaces in contact with lymphatic spaces or vessels. This suggests the reason why certain primary foci of infection (furuncles, carbuncles, etc.) are equally commonly accompanied by positive and by negative cultivations. In these cases the bacteria in the primary lesion may be limited and may not always be permitted to extend into a nearby vessel because of various reasons—mechanical and anatomic, antibody activity, etc., of course, when bacteria do not enter the circulation, bacteriemia does not occur. On the other hand, if these natural barriers do not exist, or are insufficient, bacteria enter the blood stream, and bacteriemia results. For instance, this explains the difference in clinical virulence of infections of the face, the different conceptions held in different clinics regarding association with positive blood cultures, the different opinions regarding the seriousness of these infections of the face, and the different points of view regarding the correct method of treatment, i.e., conservative treatment or incision.

(b) The thrombophlebitis in the primary lesions does not contain living, growing bacteria.

B Sterile blood cultures are associated with conditions in which the path of entry of the infection lies through the lymphatics.

C Sterile blood cultures are obtained when the portal area is interposed between the point of entry of the infection and the general circulation. This seems to be associated with an antibacterial property of the liver. This fact was first established experimentally by Wyssokowitsch in 1886, and has been corroborated by others since then.

D Sterile blood cultures may be associated with intervals between temporary states of bacteriemia. The development of secondary foci in the presence of negative blood cultures is the most powerful proof of these temporary bacteriemias. The temporary bacteriemias find their mechanisms in the repeated discharge of numbers of bacteria into the blood stream, each discharge being separated by an interval sufficiently long to allow the destruction of the organisms. Clinically, the discharge of bacteria into the circulation is often accompanied by a chill. There is abundant experimental proof (Wyssokowitsch and others) to show that the injection of living organisms into the circulation of the blood is followed by a progressive disappearance of the latter, so that while blood cultivations taken for the first hour or so after injection are positive those taken later are negative. In clinical practice it is a common occurrence for the temporary bacteriemias to be unintentionally produced by operation and other manipulations, as for example, in the

dressing of a wound, notably a wound of the bone, the passage of a sound into the bladder and other procedures. The lesson to be learned is that manipulations of the kind which are known to cause these bacteremias should be practiced with great care and circumspection, and should be avoided altogether if possible. Unnecessary and unwise squeezing and other treatment of lesions, notably of furuncles and carbuncles, especially of the face and upper lip, may convert a seemingly innocuous lesion into a fatal one complicated by a thrombophlebitis of the facial vein and of the cavernous sinus.

In the presence of positive and negative blood cultures, a progressive impoverishment of the general condition of the patient is frequently due to the magnitude and number of the various points of fixation that have occurred or to their location in important viscera or localities of the body rather than to the presence of the blood infection. Positive blood cultures are sometimes obtainable only at a late stage of the illness. Death results from either a general progression of the entire infection or from the results of any one particular manifestation, for instance, from the results of a localization in the lungs and pleura.

Character of Organisms Found on Culture—Facts obtained by studying cultures of purulent or other material (exudate) obtained from a demonstrable local focus of infection also frequently serve valuable purposes. The information can be classified as follows:

A The mere presence of organisms in the exudate serves as a means of diagnosis. The best example of this is the finding of pyogenic or other organisms in the spinal fluid.

B The character of the infecting organism frequently serves as a means of differential diagnosis and at the same time helps materially in establishing the prognosis, i. e., the demonstration of anthrax bacilli in an otherwise indifferent looking lesion changes the outlook to an extremely grave one. In other instances the character of the organism becomes important when the lesion is in a given tissue, i. e., the presence of Welch bacilli in a focus of infection in muscle tissue makes an otherwise favorable prognosis potentially fatal. Cases are constantly being seen in which it is difficult to decide whether a focus of infection has localized in a bone or in an adjacent joint. True enough, this sometimes indicates a simultaneous involvement of both, but in other cases the localization is hidden in a general inflammatory reaction. Under these circumstances, the demonstration of organisms of the staphylococcus group—*Staphylococcus aureus* especially—indicates that the chances are greatly in favor of an involvement of the bone, the demonstration of organisms of the streptococcus group would speak in favor of an involvement of the joint. The differentiation carries with it a possible therapeutic indication. Other things being equal, the demonstration of organisms of the staphylococcus group with

its consequent interpretation of a lesion of the bone would ordinarily favor exploration of the bone in cases of doubt, while the demonstration of organisms of the streptococcus group would indicate a more conservative treatment, at least as far as exploration of the bone was concerned

C Recently abdominal puncture has been practiced in cases of general peritonitis, either as a method of diagnosis in doubtful cases or as a means of differentiating a pneumococcus or streptococcus peritonitis. When these organisms are demonstrable, it indicates that the peritonitis is a metastatic one and is unassociated with a definite focus of infection in an intra-abdominal viscus which is amenable to surgical treatment, the prognosis then becomes extremely grave, in Mount Sinai Hospital the usual custom is to refuse to operate in these cases

D In infections of the middle ear the demonstration of a mucoid encapsulated coccus is commonly accompanied by a rapid destruction of tissue, which is unaccompanied by perceptible clinical or other evidence. Exploration of the mastoid is then indicated, although with other types of bacteria operation would not be considered

PORTAL OF ENTRY OF INFECTION

In any given case, a demonstrable bacteriemia may be referable to the original primary lesion at the portal of entry of the infection or to any secondary or subsidiary form of infection. Because of the thrombophlebitis which is produced at the point of fixation, secondary foci can also give rise to a bacteriemia, these include especially foci of osteomyelitis and a bacterial endocarditis

Primary bacteriemias are more commonly demonstrable and recognizable as such in cases of infection by specific organisms, as, for example, the gonococcus bacteriemia accompanying an acute gonococcus urethritis or the pneumococcus bacteriemia accompanying a pneumococcus pneumonia of the lobar type. Somewhat less commonly the primary bacteriemia is recognizable as being due to the original primary lesion because the latter is available for discovery and observation on an exposed surface of the body as for example the bacteriemia which accompanies a carbuncle or furuncle of the skin or that which accompanies streptococcus tonsillitis. Sometimes both of these factors the specificity of the organism and the location of the lesion on a surface of the body favor the recognition of the primary bacteriemia as such as for example, the bacteriemia which accompanies an anthrax lesion of the face or the bacteriemia which accompanies typhoid fever, in which the portal of entry is on the mucous surface of the ileum and the primary lesion is in Peyer's patches. Except under these specific conditions the available instances in which the demonstrable bacteriemia

can be recognized as primary and as being derived from the primary lesion at the portal of entry seem to be in the minority

In other cases distinct primary and subsidiary lesions coexist and are associated with a demonstrable bacteriemia. Then it is commonly difficult to say whether the demonstrable bacteriemia is derived from the primary or from the secondary lesion. The best examples of this difficulty are found in conditions of the ear in which a primary lesion is found in a complicating thrombosis of the lateral sinus, and secondary lesions are found in a bone or in a joint. Here the primary lesion remains a constant factor even in the presence of subsidiary foci which can themselves originate bacteriemias. Even after the jugular vein has been efficiently tied a bacteriemia may still be derived from extension of the primary thrombus along the petrosal sinuses, and it is a nice distinction to integrate a bacteriemia properly between a subsidiary focus elsewhere in the body and the primary lesion in the lateral and petrosal sinuses. Some facts pertinent to this distinction will presently be referred to in discussing the situations which may arise in acute osteomyelitis.

Lastly, in still other cases a focus of infection is present which is distinctly a metastatic lesion, and which is accompanied by a bacteriemia. In the one group of such cases a primary lesion is sometimes demonstrable as a definitely healed lesion. A common example of this clinical fact is found in cases of acute hematogenous renal infections (hematogenous multiple renal infarcts), frequently, indeed, the site of the original furuncle is still recognizable in a recently healed scar. In the second and much more common group of these cases, the primary lesion is undemonstrable. The commonest example of this status is found in cases of acute osteomyelitis. In the presence of any of these combinations experience leads one to assume that for clinical purposes all of these bacteriemias should be associated with the demonstrable metastatic lesion. Fairly complicated situations can and do arise, and the lines of thought which one follows are best illustrated in the cases of acute osteomyelitis.

In many of the cases only a single focus of osteomyelitis is demonstrable. In most of the cases in this group, a comparatively small number of bacteria are demonstrable in the circulation of the blood (plate culture method). Should the bacteriemia disappear before operation spontaneously and fairly promptly, one may assume that the bacteriemia was caused by the undiscoverable primary lesion to which the demonstrable focus of osteomyelitis was subsidiary.

If the bacteriemia persists, and if it disappears promptly after an efficient operation in which the entire focus of infection in the bone is removed, the assumption seems justified that the demonstrable bacteriemia was derived from the thrombophlebitic lesion in the focus

of infection in the bone. This is the criterion which prompts active radical operative treatment in cases of osteomyelitis associated with bacteriemia.

In some of the cases, however, bacteriemia persists after operation. When the surgeon is certain that the lesion of the bone has been so thoroughly removed that it cannot cause bacteriemia, and when the appearances of the wound in the bone corroborates this impression, the bacteriemia should be considered as an indication that some other focus exists which must be found and removed in order to render the blood sterile. Many times this proves to be the case, but when it does not, the original focus of osteomyelitis should be examined again and revised operatively.

If bacteriemia persists, and if the number of demonstrable bacteria still is comparatively small, other foci or lesions capable of causing bacteriemia should be looked for. In the absence of any such demonstrable lesion, the explanation of the bacteriemia cannot be decisive, although it must necessarily be assumed under the circumstances that the original focus continues to discharge bacteria into the blood stream.

In the meanwhile, other foci should be looked for, especially during the continuation of the bacteriemia, which may subsequently be found to be due to some complicating factor unrelated to the focus of infection in the bone (intercurrent disease or some other condition). When the bacteriemia cannot be adequately explained and when it continues to exist, a bacterial endocarditis should be looked for. The presence of this condition is the most serious complication possible, and the prognosis is grave, operation on any local focus is futile in the presence of a bacterial endocarditis, and a fatal outcome should be expected.

The explanation of the bacteriemia becomes a matter of exclusion when several foci of infection coexist. Rules similar to those outlined in the foregoing paragraph apply.

TREATMENT FOR THE LOCAL LESION

Treatment for the local lesion should be based on (1) a consideration of the mechanism by which the focus is produced, (2) the character of the lesion which is produced as determined by all available knowledge, and (3) the magnitude of the infection in association with the absence or presence of bacteriemia. Multiple foci should be treated individually along similar lines and in accordance with the points of view expressed.

A Other things being equal, the absence of a demonstrable bacteriemia or general blood infection indicates that a conservative attitude can be assumed in deciding the correct method of surgical treatment of the local focus. The immediate important results of this conservative attitude include (1) the performance of a much less severe—frequently a minor—primary operation, (2) much less chance of the spreading of

the thrombophlebitic or thrombo-arteritic process with all the consequences outlined, (3) frequent conservation of important organs or tissues, and (4) frequent avoidance of unnecessary complications

B Other things being equal, the presence of a demonstrable bacteriemia or general blood infection indicates a dangerous and possibly progressive lesion, it also indicates that an urgent effort, commensurate with the severity of the infection, should be made to remove the local focus as early and as completely as possible before the spreading infection does irreparable damage to the endocardium or to some important organ or locality. All of the information classified in the previous part of this and in other papers as regards the clinical and therapeutic significance of a bacteriemia or general blood infection should be considered at this time and judgments formed and indications met accordingly.

The important indication is to remove the local focus of infection as completely as possible. Frequently, conservative treatment should be replaced by radical removal of tissue into healthy areas in an attempt to reach a point distal to the thrombophlebitic lesion. The difficulty at these early stages is the impossibility of recognizing the limits of the lesion, and much wider excisions of tissue must therefore necessarily be done than would otherwise be necessary. There are times and localities in which radical removal of the thrombophlebitic focus is not technically feasible, under these circumstances, as much as possible should be done in this direction, ample drainage should be secured as the next best treatment. A good deal must be entrusted to nature's efforts to dissipate the bacteriemia spontaneously.

Local anesthesia should never be employed in operating on foci of infection in the skin. The method lends itself to the spreading of the lesion and is equally at fault with rough manipulations or squeezing of the tissues near the infected areas. In operating on foci of infection in deep organs or tissues, local anesthesia may of course be used for the outer wound.

The phenomena associated with and accompanying a bacteriemia sometimes occur after operation—so-called "operating room infection"—in divers parts of the body. The accident is undoubtedly associated with the vascular thromboses which are a necessary incident in the healing of all operatively produced wounds. The infection of the latter does not always predicate an introduction of organisms from without, but the bacteria may come from unrecognized foci of infection pre-existing in the body, as, for instance, in the tonsils, the wound then becomes a secondary focus. This is the most important reason for adequate physical examination of all patients before operation, and search should be especially directed toward otherwise obscure areas of the body.

As a general rule, postoperative infections, with demonstrable bacteriemia, are extremely serious and usually terminate fatally. Clinically, the patient has high fever and chills, the chills usually occur at irregular intervals whenever swarms of bacteria are being sent into the circulation. The local area of the operative wound need not necessarily show more evidences of change than are seen under more happy circumstances, and it is always impossible to discover any other focus of infection which could account for the bacteriemia.

In certain areas of the body and after certain operations, for instance in the pelvis, and after amputations of the breast for carcinoma, the proximity of large veins to the operative field should make one suspect that the circumstances outlined in the foregoing paragraph are associated with an infected thrombosis of the adjacent vascular channels. Exploration of these venous channels is urgently indicated, when the thrombi are found, these should be removed and the veins tied on their distal side. The latter operation will succeed in direct proportion to the shortness of time during which the thrombi has been allowed to feed bacteria into the blood stream, success will not always follow when secondary foci have been established, and never when the endocardium becomes secondarily involved.

The phenomena accompanying the spread of the thrombophlebitis are apt to occur after operation, particularly in tissues provided with an abundant vascular plexus, for example, in bone tissue. Clinically, these are recognizable by the continuation of the subjective and objective phenomena or by recrudescences or exacerbations of the process. Much more serious effects can occur in infections of the skin—furuncles, carbuncles, etc.—after operation, and the danger of spreading an old thrombophlebitis or causing a new one is directly proportionate to the proximity of the local focus of infection to an adjacent vein. I have referred to this previously in discussing local infections of the face and upper lip. For this reason, conservatism is indicated in treatment for local infections of this kind.

CHANGES IN THE CHEMISTRY OF THE CONTENTS OF THE STOMACH FOLLOWING GASTRIC OPERATIONS *

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Surgeons advocating radical operation (Lewisohn¹ and de Takata²) and even those advocating conservative methods (Portis and Portis³) in the treatment of gastric and duodenal ulcers agree that gastrectomy produces a lower acidity or an anacidity in the contents of the stomach. The mechanism concerned in bringing about this change, however, is a subject of controversy. Deaver and Reimann⁴ stated that the resection of the antrum does away with the area of the stomach mucosa that secretes acid. This is contrary to anatomic and physiologic facts. The antrum is lined by pyloric glands which contain no or only a few, acid cells (Steinberg⁵). These glands secrete only an alkaline form of mucus (Babkin⁶). The relation of the mucosa of the antrum to the secretion of gastric juice was first called to our attention by Edkins⁷. This investigator found that extracts of the mucosa of the antrum mixed with other substances, such as peptone and water, and then injected into the blood stream produced the secretion of gastric juice. Edkins⁷ was of the opinion that this action of the mucosa of the antrum was specific. Later, Keeton and Koch⁸ found that extracts of other glands injected

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1 Lewisohn, R. The Relation of Postoperative Achlorhydria to the Cure of Gastric and Duodenal Ulcers, *Surg Gynec Obst* **44** 344, 1927

2 De Takata, G. The Perverted Physiology of the Stomach after Gastric Operations, *Am J M Sc* **172** 45, 1926

3 Portis, B, and Portis, S. Effects of Subtotal Gastrectomy on Secretion, *J A M A* **86** 836 (March 20) 1926

4 Deaver, J B, and Reimann, S P. Subtotal Gastrectomy, *J A M A* **85** 1619 (Nov 21) 1925

5 Steinberg, M E. Stomach Mucosa in Ulcer and in Carcinoma, *Arch Surg* **14** 991 (May) 1927

6 Babkin, B P. Die aussere Sekretion der Verdauungsdrusen, Berlin, Julius Springer, 1914, pp 118, 119

7 Edkins, J S. The Chemical Mechanism of Gastric Secretion, *J Physiol* **34** 133, 1906

8 Keeton, R W, and Koch, F C. The Distribution of Gastrin in the Body, *Am J Physiol* **37** 481, 1915

into the blood stream also caused the secretion of gastric juice. Tomaschewsky⁹ found that gastrin was distributed uniformly throughout the mucosa of the stomach. The work of Edkins,⁷ however, stimulated an interest in the rôle that the mucosa of the antrum may play in the complicated mechanism of gastric secretion.

According to Pawlow¹⁰ and his school, there are two main phases of gastric secretion. The first is the psychic phase, which is responsible for a great deal of the secretion of gastric juice, and which is brought about by the animal seeing, smelling, tasting and chewing food. The chemical phase is characterized by a long latent period. It is believed that the secretion from the glands of the fundus is brought about through the stimulation of the mucosa of the antrum. The flow of gastric juice can also be inhibited by the various foodstuffs coming in contact with the duodenal mucosa. In the experiments dealing with the mechanism of secretion concerned in the chemical phase, Krshyschkowsky¹¹ and Gross¹² have divided the dog's stomach into the pars pylorica and the fundus. In other experiments, Gross¹² has separated the duodenum from the antrum so as to study the effect of substances on the gastric secretion when they are introduced directly into the duodenum. The dogs were kept alive by an external gastro-enterostomy (fig 4).

It was found that neutral fat, oleic acid, soaps, soda and physiologic sodium chloride solution, when introduced into the duodenum, appear to have an inhibitory influence on the secretion from the mucosa of the fundus. On the other hand, meat extracts, water, salt solution, pancreatic juice, bile, oleic acid and lactic acid, also soaps, dextrin and dextrose solution, when introduced into the antrum, stimulate the secretion of the glands of the fundus. Krshyschkowsky,¹¹ Zeljony¹³ and Gross¹² have introduced meat, bread, milk, water, lactic acid, bile, Liebig's beef extract and peptone into the fundal part of a dog's stomach. These substances remained in the fundus for two hours and longer without producing any secretion of gastric juice.

Babkin⁶ concluded that the chemical irritation of the surface of the mucosa of the fundus of the stomach does not bring forth the secretion from its glands.

9 Tomaschewsky, Z. Ueber die chemischen Erreger der Magendrüsens. *Arch f d ges Physiol* **170** 260, 1918.

10 Pawlow, I. P. *The Work of the Digestive Glands*, London, Charles Griffith & Company, 1910.

11 Krshyschkowsky, quoted by Babkin, B. P. *Die aussere Sekretion der Verdauungsdrusen*, Berlin, Julius Springer, 1914, p. 126.

12 Gross, W. Beitrag zur Kenntnis der Sekretionsbedingungen des Magens nach Versuchen am Hund, *Arch f Verdauungskr* **12** 507, 1906.

13 Zeljony, quoted by Babkin, B. P. *Die aussere Sekretion der Verdauungsdrusen*, Berlin, Julius Springer, 1914.

Ivy¹⁴ has emphasized that there is an intestinal phase of gastric secretion. He separated the stomach from the esophagus and duodenum. One end of the stomach was closed and the other end was brought outside by a fistula. The dog was fed in the normal manner and the food was passing from the mouth to the esophagus which was anastomosed to the duodenum. From two to four hours after the dog was fed, the isolated stomach secreted copiously. Ivy¹⁴ has also demonstrated the humoral mechanism in gastric secretion. He was able to isolate the pouch of the stomach and separated it from the nerve and blood supply of the main part of the stomach. He transplanted this pouch under the mammary gland of a dog and found that when the dog was fed the transplanted pouch secreted gastric juice.

Since the European surgeons have begun to treat gastric and duodenal ulcers by resection of the stomach and have noted the striking change in the chemistry of the contents of the stomach, they were stimulated to theorize as to the cause of the reduction in the acidity. Lorenz and Schur¹⁵ have reviewed a series of their material following gastrectomy. They have noticed that the size of the antrum removed was directly proportional to the reduction in the acidity. They laid emphasis on the fact that the removal of the antrum does away with the part of the stomach which is indirectly responsible for the chemical phase of gastric secretion. These authors did not believe that the neutralization of the stomach contents by regurgitation of the alkaline juices from the intestine could play any part in producing the striking change. Later, some experimental work was undertaken by Smidt,¹⁶ who utilized the methods of the Pawlow school. He formed a Pawlow pouch and then resected the antrum and studied the change produced. He came to the conclusion that the removal of the antrum, especially after the method of Billroth I, reduces the secretion of gastric juice to a minimum. Two years later in an experimental study, Portis and Portis,³ using the same methods as Smidt,¹⁶ demonstrated that after gastrectomy the Pawlow pouch secretes a gastric juice high in acidity. They were of the opinion that the neutralization of the contents of the stomach by regurgitation of the intestinal juices is the most important factor in changing the acidity of the contents of the stomach after resection of the antrum.

14 Ivy, A. C. Contribution to the Physiology of the Stomach, *J. A. M. A.* **85** 877 (Sept. 19) 1925.

15 Lorenz, H., and Schur, H. Unsere Erfahrungen über den Wert der Antrumresektion bei der Behandlung des Ulcus Pepticum, *Arch. f. klin. chir.* **119** 239, 1922.

16 Smidt, H. Experimentelle Studien am nach Pawlow isolierten kleinen Magen über die sekretorische Arbeit der Magendrüsen nach Resektionen Billroth I und II, sowie nach der Pylorusausschaltung nach V. Eiselsberg **135** 26, 1923.

It is evident that investigators using the same methods have disagreed as to the real mechanism concerned in bringing about the change in the chemistry of the gastric contents after resection of the antrum. Smidt,¹⁶ using the same methods as Portis and Portis,³ came to the conclusion that resection of the antrum reduces the secretion of gastric juice, while Portis and Portis³ believed that the neutralization of the contents of the stomach is the biggest factor in bringing about the change in the acidity. It remained for us to find other methods of experimentation in addition to the methods already in use in order to throw more light on the following problem: Does the removal of the antrum do away indirectly with the secretion of gastric juice in the manner of eliminating the chemical phase, or does a gastro-intestinal anastomosis after the resection bring about a change in the emptying time of the

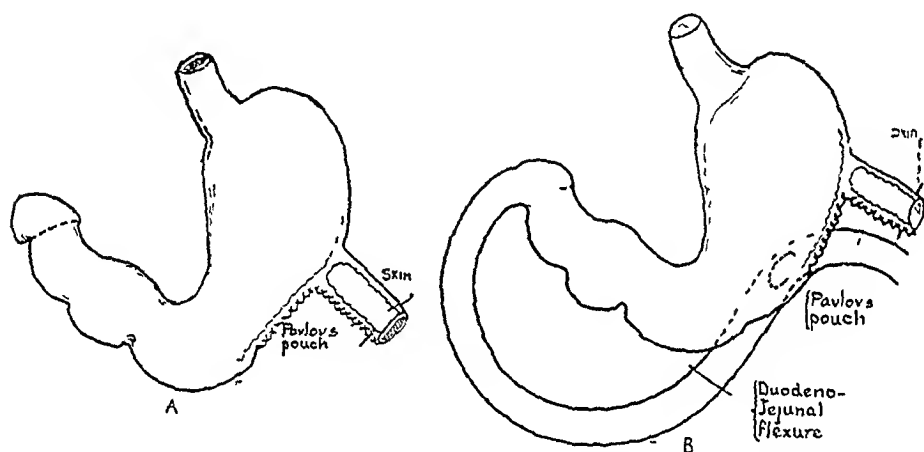


Fig 1—A, normal stomach with Pawlov pouch, B, normal stomach with Pawlov pouch and a posterior gastro-enterostomy

stomach and in the regurgitation of the alkaline intestinal contents to such a degree that the changed chemistry is due to neutralization?

EXPERIMENTAL METHODS

In the course of our experiments, we have also studied the changes that are induced in the chemistry of the contents of the stomach by gastro-enterostomy alone. This part of our study, however, was incidental, since in our plan of work we have performed a gastro-enterostomy before removing the antrum. We shall discuss briefly the phase of gastro-enterostomy only, as it is related to our chief problem, since one of us (Burget and Steinberg¹⁷) has already published an experimental study dealing with the regurgitation of intestinal contents after gastro-enterostomy.

17 Burget, G. E. and Steinberg, M. E. Studies on the Physiology of Gastro-Enterostomy, *Am J Physiol* 60 308, 1922

In the first series of experiments, we studied the change in the quantity and the chemistry of secretion as it is affected by a gastro-enterostomy

For this purpose, we made a Pawlow pouch from the fundus of the stomach in the manner described by Pawlow (fig 1). We fed the dog 200 Gm of cooked meat and noticed the normal response of the glands from the pouch (table 1 *A*). Later, we performed a gastro-enterostomy on the same animal (fig 1 *B*) and fed it the same type of meal and examined the gastric juice obtained from the Pawlow pouch (table 1 *B*). Tables 1 *A* and 1 *B* show that there was no appreciable change either in the acidity or in the peptic activity of the gastric juice secreted by the mucosa of the fundus before or after gastro-enterostomy. There was a slight diminution in the quantity of gastric juice secreted in the first three hours in the dog with the gastro-enterostomy.

TABLE 1 (*Dog 7*)—Normal Response of Glands from Pouch

A					B				
Normal Stomach with Pawlow Pouch (Fig 1 <i>A</i>)					Gastrostomy and Pawlow Pouch (Fig 1 <i>B</i>)				
(200 Gm of Cooked Meat Given March 6, 1924)					(200 Gm of Cooked Meat Given April 30, 1924)				
Hours	Cc Secreted in One Hour	Free Acidity	Total Acidity	Pepsin Mm	Hours	Cc Secreted in One Hour	Free Acidity	Total Acidity	Pepsin Mm
1	30	0.3098	0.3163	0.2	1	48	0.3737	0.4831	3.0
2	60	0.3731	0.4649	2.0	2	30	0.3919	0.4922	3.0
3	65	0.4102	0.4922	4.0	3	25	0.4010	0.4922	3.5

In the second series of experiments, we attempted to study the effects that the removal of the antrum may have on the change in the secretion of gastric juice.

First, we performed a Pawlow pouch (fig 2 *A*). After the dog recuperated from the operation, we fed him a meal consisting of 200 Gm of cooked meat and noticed the response of the Pawlow pouch (table 2 *A*). Later, we removed the antrum of the stomach and anastomosed the fundus to the duodenum (fig 2 *B*). After the dog recuperated sufficiently from the second operation, we gave him the same meal as on the previous occasion and noticed the response of the Pawlow pouch (table 2 *B*). Tables 2 *A* and 2 *B* indicate that the acidity and the concentration of pepsin of the gastric juice was not changed after removal of the antrum. It is to be noted, however, that the quantity secreted by the pouch on the same meal, after removal of the antrum, was reduced in the first three hours to less than half of the response in the normal stomach.

We were somewhat delayed in our work, and in the meantime Smidt¹⁶ and Portis and Portis³ have published a report of their experiments utilizing the same methods. We did not think that it would be possible to solve all the phases of the problems concerned in our work by utilizing the Pawlow pouch method only, and we therefore proceeded to other forms of experimentation.

The third method of experimentation was based on the work of Boldyreff¹⁸

This author introduced 0.5 per cent of hydrochloric acid into the stomach of a dog and found that after an hour the contents of the stomach were reduced to about 0.15 per cent hydrochloric acid. He concluded that when the acid of the contents of the stomach is raised to a certain point it is neutralized by the regurgitation of the pancreatic juice, bile and succus entericus into the stomach. Burget and Steinberg¹⁷ repeated Boldyreff's experiments on dogs in the normal state, and have also studied the regurgitation in dogs on which gastro-enterostomy had been performed. These authors found that after gastro-enterostomy duodenal regurgitation takes place within fifteen minutes after the introduction of from 100 to 150 of 0.5 per cent hydrochloric acid 0.1 per cent in only thirty or forty-five minutes. In our present study, we have introduced 200 cc of 0.5 per cent hydrochloric acid into the intact stomach of a dog (fig 3 A) and have aspirated the

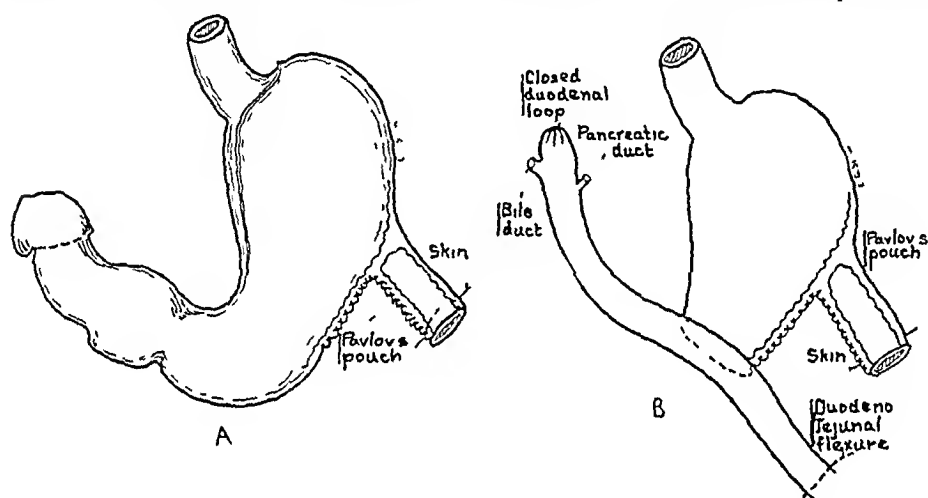


Fig 2—A, normal stomach with Pawlov pouch, B, Pawlov pouch with antrum removed and gastrojejunostomy

TABLE 2 (Dog 3)—Effects of Removal of Antrum on Secretion of Gastric Juice

A Normal Stomach with Pawlov Pouch (Fig 2 A)					B Antrum Resected and Pawlov Pouch Intact (Fig 2 B)				
(200 Gm of Cooked Meat Given Jan 13, 1924)					(200 Gm of Cooked Meat Given Jan 27, 1924)				
Hours	Cc Secreted in One Hour	Free Acidity	Total Acidity	Pepsin Mm	Hours	Cc Secreted in One Hour	Free Acidity	Total Acidity	Pepsin Mm
1	20	0.2371	0.3372		1	30	0.3098	0.3163	0.2
2	45	0.1003	0.2918	10	2	15	0.1732	0.2280	1.5
3	23	0.2918	0.4922	11	3	0.2	0.3100	0.4538	

contents every fifteen minutes, examining them for free acidity, total acidity and visible bile. We found that it takes from an hour to seventy-five minutes for the 200 cc of 0.5 per cent hydrochloric acid to be reduced to 0.15 per cent hydrochloric acid or less (table 3 A). We then performed a gastro-enterostomy (fig 3 B). After the dog recuperated sufficiently, we repeated the regurgitation experiments as

18 Boldyreff, W. Einige neue Seiten der Tätigkeit des Pankreas, *Ergebn d Physiol* 77 121, 1911

in the normal animal (table 3 *B*). After gastro-enterostomy was performed, visible bile was immediately found in the stomach and it took only about thirty or forty-five minutes for the 0.5 per cent hydrochloric acid to be reduced to 0.15 per cent hydrochloric acid or less (table 3 *B*). We then removed the antrum from the stomach of the dog, leaving the old gastro-enterostomy intact (fig 3 *C*), and repeated the regurgitation experiments as on the normal dog (table 3 *C*). With the antrum removed, bile appeared in the contents of the stomach immediately. The 0.5 per cent hydrochloric acid was reduced to 0.14 per cent hydrochloric acid after thirty minutes, and no acid was demonstrated after forty-five minutes (table 3 *C*). The acid contents left the stomach much faster after the antrum was removed (table 3 *C*) than in the stomach in which the gastro-enterostomy only had been performed (table 3 *B*). Since the gastro-enterostomy opening was the same before and after the stomach was resected, it is difficult to explain why the process of neutralization should be much faster after the antrum was removed. It is possible that when the stomach is intact, the peristaltic

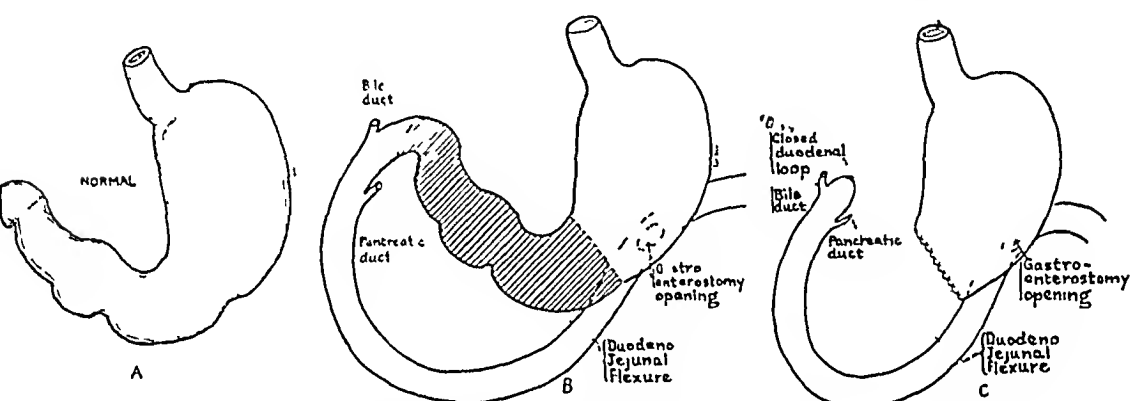


Fig 3—*A*, normal stomach, *B*, posterior gastro-enterostomy, *C*, same as *B*, except that the antrum has been removed

waves propel the contents into the antrum, where they are momentarily arrested. With the antrum removed, the contents of the stomach are propelled directly into the gastro-enterostomy opening. Again, the injury to the structures involved in the performing of a gastrectomy may affect the nerve supply of the stomach to such an extent that its motor activity will be changed.

The fourth method of experimentation was as follows:

We divided the dog's stomach, separating the antrum from the fundus, in such a way that the fundus and the antrum were open to the outside by external fistulas (fig 4). In this way the fundus was directly connected to the esophagus, and the duodenum was connected with the antrum. The dog was given nothing but milk and water and the contents of the fundus were transmitted to the antrum through a glass tube from the outside (fig 4). After the dog recuperated sufficiently, we performed the following experiments. At first we took out the tube and washed the fundus and antrum with physiologic sodium chloride solution. We then introduced 10 Gm of Liebig's beef extract dissolved in 150 cc of water into the fundus and aspirated the contents from the fundus and from the antrum every fifteen minutes (table 4 *A*). The results emphasize the fact that the fundus continuously secreted a high degree of acid, while in the antrum free acid was not found. On the following day, we took the tube out and washed the antrum and fundus with physiologic sodium chloride solution and introduced

TABLE 3 (Dog 16 B)—Regurgitation Experiment

A				B				C			
Normal Stomach (Fig 3 A)				Gastro-Enterostomy (Fig 3 B)				Antrum Removed (Fig 3 C)			
200 Cc of 0.5 per Cent Hydrochloric Acid Introduced Into the Stomach at 12 40 p m, Oct 29, 1926				200 Cc of 0.5 per Cent Hydrochloric Acid Introduced Into the Stomach at 12 55 p m, Nov 12, 1926				200 Cc of Hydrochloric Acid Introduced Into the Stomach at 1 30 p m, Oct 2, 1926			
Time of Examination	Free Acidity	Total Acidity	Comment	Time of Examination	Free Acidity	Total Acidity	Comment	Time of Examination	Free Acidity	Total Acidity	Comment
12 12	0.3281	0.1558		1 10	0.2006	0.2827	Bile +	1 45	0.1824	0.2644	Bile +
1 10	0.3007	0.4375		1 25	0.1550	0.2280	Bile +	2 00	0.1459	0.1824	Bile + +
1 25	0.2644	0.3403		1 40	0.0638	0.1459	Bile +	2 15	No free hydrochloric acid	0.0638	Bile + + + +
1 40	0.0912	0.2006	Bile +	1 35	0.0456	0.1368	Bile + +				
1 55	0.0775	0.1611	Bile	2 10	0.0638	0.1276	Bile + +				
2 10	0.0517	0.1276	Bile	2 25		0.0912	Bile + +				

10 Gm of Liebig's beef extract, in 150 cc of water, into the antrum (fig 4). We aspirated the contents from the antrum and from the fundus at fifteen minute intervals. From table 4 B, it is evident that when the beef extract was introduced into the antrum the fundus secreted free acid continuously, the highest being 0.1824, while there was no free acid in the antrum.

Lorenz and Schui¹⁵ and Gross¹² have emphasized the importance of the antrum in the chemical phase of the secretion of gastric juice. In our experiments, we confirmed the work of Gross¹² and Kishy-schkowsky¹¹ that when certain substances were introduced into the antrum the fundus secreted a gastric juice of considerable acidity. We have, however, also demonstrated that when certain substances are introduced into the fundus alone, the mucosa of the fundus responds with

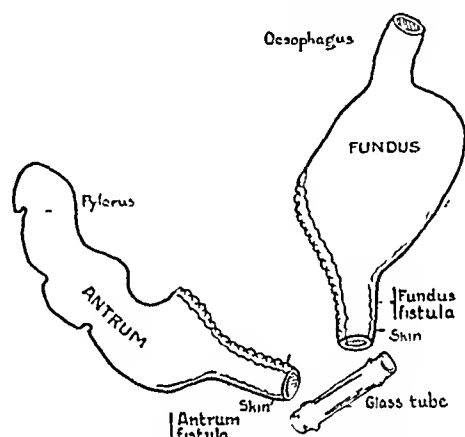


Fig 4—Stomach divided into antrum and fundus and both brought to the outside by means of fistulas

TABLE 4 (Fig 4)—*The Relation of the Antrum to the Secretion of Gastric Juice (Fundus separated from Antrum and Both United by External Gastro-Enterostomy)*

A			B		
150 Cc of Liebig's Beef Extract Introduced Into the Fundus at 2 00 p m, April 6, 1927, and Both Fundus and Antrum Aspirated at Fifteen Minute Intervals			150 Cc of Liebig's Beef Extract Introduced Into the Antrum at 6 00 p m, April 7, 1927, and Both Fundus and Antrum Aspirated at Fifteen Minute Intervals		
Time of Examination	Fundus Free Acidity	Antrum Free Acidity	Time of Examination	Fundus Free Acidity	Antrum Free Acidity
2 15	0.2188	None	6 15	0.1185	None
2 30	0.2736	None	6 30	0.1824	None
2 45	0.2553	None	6 45	0.1550	None
3 00	0.1185	None	7 00	0.1454	None

a higher acidity than when the same substances are introduced into the antrum. This is contrary to the experiments of Gross¹² and Kishy-schkowsky,¹¹ who claim that the introduction of substances into the fundal part of the stomach does not bring about the secretion of gastric juice.

In the previous series of experiments, we were able to demonstrate that after the antrum was resected, the fundus secreted gastric juice of normal acidity, though it was less in amount (tables 2 *A* and 2 *B*). When certain substances were introduced into the antrum (fig 4), the fundus secreted a gastric juice lower than normal in acid concentration (table 4 *B*). In the experiments in regurgitation (figs 3 *A*, 3 *B* and 3 *C* and tables 3 *A*, 3 *B* and 3 *C*), we found that the removal of the antrum causes a rapid emptying of the contents of the stomach and a decisive and almost immediate neutralization of these contents through the regurgitation of the intestinal juices. It remained to be determined which factors are more important in bringing about the change in the chemistry of the contents of the stomach. Does a gastrectomy eliminate what is known as the chemical phase of secretion of gastric juice, or does it change the anatomic and physiologic factors in such a way as to bring about the reduction in acidity by the neutralization through the influx of the intestinal contents?

We performed the regurgitation experiments (table 5 *A*), and also gave the animal a test meal containing 20 Gm of Liebig's beef extract diluted in 300 cc of water (table 6 *A*). After finding out the response to the intact stomach (fig 5 *A*, tables 5 *A* and 6 *A*), we resected the antrum and administered the same test meals as in the experiment on the normal stomach (fig 5 *B*, tables 5 *B* and 6 *B*).

After the dog had sufficiently recuperated from the operation for the resection of the antrum (fig 5 *B*), we divided the duodenum at the point above the anastomosis and united the distal part of the duodenum with the ileum¹⁹. In this way, all the pancreatic juice and bile were directly transmitted to the ileum and could not regurgitate into the fundus of the stomach (fig 5 *C*).

In the regurgitation experiments, after the stomach was resected, the neutralization took place rapidly (table 5 *B*). After the duodenal contents were diverted to the ileum, a high acidity persisted until no more acid contents could be obtained from the stomach (table 5 *C*). The same result, only not so striking, is apparent from tables 6 *A* and 6 *B*, in which the animal was given a meal containing 20 Gm of Liebig's beef extract dissolved in 300 cc of water. Table 6 *A* showed that after this meal was given the normal stomach responded with the usual acidity of the contents of the stomach (free acid, from 0.1003 to 0.2188). After the stomach was resected and the duodenal contents diverted (fig 5 *C*,

19 The method of diverting the duodenal contents into the ileum is original with us and was suggested by the senior author to Professor Burget of the Physiology Department of the University of Oregon Medical School six years ago. We intended to employ this method for the purpose of studying the etiology of duodenal and gastric ulcers. Since then, however, Mann has published his work utilizing the same principle, *Ann Surg* 77:409, 1923.

TABLE 5 (*Dog 40 B*)—*Regurgitation Experiment*

A				B				C			
Normal Stomach (Fig 5 A)				Antrum Removed (Fig 5 B)				Antrum Removed and Duodenal Contents Diverted to the Ileum (Fig 5 C)			
200 Cc of Hydrochloric Acid Introduced Into Stomach at 1 00 p m, May 16, 1927				200 Cc of 0.5 per Cent Hydrochloric Acid Introduced Into the Stomach at 1 15 p m, June 1, 1927				200 Cc of 5.0 per Cent Hydrochloric Acid Introduced at 1 15 p m June 10, 1927			
Time of Examination	Free Acidity	Total Acidity	Comment	Time of Examination	Free Acidity	Total Acidity	Comment	Time of Examination	Free Acidity	Total Acidity	Comment
1 15	0.2736	0.1375		1 30	0.2280	0.3093		1 30	0.3372	0.1102	None
1 30	0.2553	0.3554		1 45	0.2280	0.2736		1 45	0.2553	0.3516	None
1 45	0.2553	0.3163		2 00	0.1276	0.1824	Bile ++	2 00	0.2371	0.3372	None
2 00	0.2462	0.3190		2 15	0.0729	0.0912	Bile +++	2 15	0.2162	0.3463	None
2 15	0.1915	0.3094	Bile +	2 30		0.0825	Bile ++	2 30	0.2371	0.3251	None
2 30	0.1641	0.2553	Bile +					2 45	No more stomach contents		

table 6 C), and the dog was given the same meal consisting of Liebig's beef extract, a free acidity that was higher than that in the intact stomach persisted for a long time (free acidity, from 0.1915 to 0.2736)

It is evident that when the antrum is resected and the pancreatic juice and bile are diverted to the ileum (fig 5 C) and the dog is given a standard meal, there is a constant free acidity, in spite of the fact that the antrum is totally removed. Without doubt, this demonstrates that after the antrum is removed, the changed chemistry of the contents of the stomach is chiefly due to the regurgitation of the alkaline juices of the duodenum into the stomach.

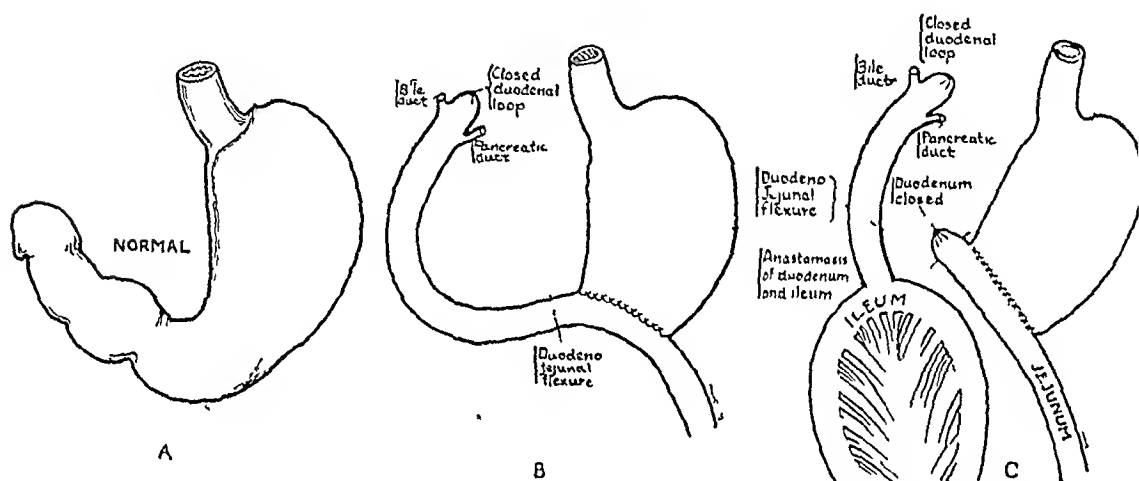


Fig 5—A, normal stomach, B, antrum removed and fundus anastomosed to the jejunum, C, same as B, except that the duodenum has been divided above the anastomosis and united to the ileum. The duodenal contents are emptying directly into the ileum.

TABLE 6 (Dog 40 B)—Test Meal Experiment

A Normal Stomach (Fig 5 A)			B Antrum Removed (Fig 5 B)			C Antrum Removed and Duodenal Contents Diverted to the Ileum (Fig 5 C)		
20 Gm of Liebig's Beef Extract in 300 Cc of Water Given at 12.45 May 18, 1927			20 Gm of Liebig's Beef Extract in 300 Cc of Water Given at 10.25 a.m., May 31, 1927			20 Gm of Liebig's Beef Extract in 300 Cc of Water Given at 9.30 a.m., July 1, 1927		
Examination	Free Acidity	Total Acidity	Examination	Free Acidity	Total Acidity	Examination	Free Acidity	Total Acidity
1.00	0.1459	0.2162	10.40	0.1824	0.2736	9.15	0.2553	0.4010
1.15	0.1185	0.2371	10.55	0.1459	0.2371	10.00	0.2553	0.4010
1.30	0.1824	0.2736	11.10	0.1641	0.2162	10.15	0.2162	0.3372
1.45	0.1915	0.3372	11.25	0.1185	0.2041	10.30	0.2553	0.3372
2.00	0.2188	0.3554	11.40	0.1641	0.3007	10.45	0.2736	0.3919
2.15	0.1732	0.3190	11.55	0.1185	0.1915	11.00	0.2188	0.3372
2.30	0.1550	0.2918	12.10	0.1368	0.2188	11.15	0.2007	0.2918
2.45	0.1185	0.1824	12.25	0.1094	0.1732	11.30	0.2006	0.2527
3.00	0.1003	0.1185				11.45	0.1915	0.2736
						12.00	No more could be aspirated	

CONCLUSIONS

1 After a gastro-enterostomy is performed, the secretion of gastric juice remains of the same concentration in acidity, but, as shown by the Pawlow pouch method, the amount of secretion is slightly lessened. The contents of the stomach are neutralized to a certain extent by the regurgitation of the intestinal contents.

2 We have been able to demonstrate that when the fundus is separated from the antrum and various substances are introduced into the fundus, the glands of the fundus respond with the secretion of gastric juice of high acidity. This is contrary to the observations of Krshyschkowsky,¹¹ Gross,¹² and Zeljony,¹³ who stated that irritation of the surface of the fundal mucosa of the stomach does not bring forth the secretion from its glands.

3 After the antrum is removed, free acidity of the contents of the stomach is considerably reduced or is entirely absent. The mechanism concerned in this process is due to two factors. The removal of the antrum eliminates a part of the stomach from which surface absorption of foodstuffs stimulates the secretion from the fundal glands. The biggest factor in the reduction of acidity after resection of the stomach is the neutralization of the contents of the stomach by the influx of the alkaline juices from the intestine. We have demonstrated this definitely, since after the antrum is removed and the bile and pancreatic juice are diverted to the ileum the acidity in the fundus is high and persists for a long time.

4 The stomach is usually divided into two distinct parts—the proximal, which is the largest and which is spoken of as the fundus and corpus, lined by the fundus glands which secrete acid and pepsin, the distal, or the smallest part, which is spoken of as the antrum or pars pylorica. This part is lined by the pyloric glands which do not secrete acid. It is therefore contrary to all physiologic and anatomic facts for surgeons and clinicians to state that by removing the antrum the area of the stomach secreting acid is also removed.

MECHANISM AND TREATMENT OF EXPERIMENTAL SHOCK

I SHOCK FOLLOWING HEMORRHAGE *

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DEFINITION

Many syndromes are grouped by investigators and clinicians under the general term "shock" Since the word has various connotations for different persons, it might well be discarded from medical nomenclature However, no satisfactory synonym is available, and the widespread clinical use of the term seems to warrant its retention

Throughout this and subsequent publications, "shock" is used to denote a condition of acute circulatory failure characterized by prostration, apathy or stupor, tachycardia with feeble, regular pulse and, in many instances, diminished blood pressure The temperature of the body is often subnormal Pallor and slight cyanosis are usually present Edema, visceral congestion and accumulations of fluid in the serous cavities do not occur in shock The latter signs are characteristics of chronic circulatory failure ("cardiac decompensation," "congestive failure," etc) Much confusion has resulted from a lack of complete differentiation between these two general conditions, which not only are different as to chronicity and etiology, but, as will be demonstrated, are dissimilar in regard to pathologic physiology and response to treatment

INTRODUCTION

Shock is generally recognized to be a group of symptoms and not a disease This syndrome is encountered more often than any other in surgical patients The more common causes of clinical shock are the following (1) acute hemorrhage, (2) prolonged anesthesia, (3) extensive wounds, (4) any acute infection in the terminal stages, (5) pulmonary embolism, (6) coronary occlusion, (7) collapse caused by heat, (8) excessive manipulation of abdominal viscera at operation, (9) fractures of long bones and (10) moribund states from any cause Among the more important procedures which may produce experimental shock are (1) the administration of histamine, (2) the intravenous administration of fat and (3) excessive hyperventilation of the lungs

In spite of the many important investigations of shock particularly of the traumatic type which have been made in the past ten years, the disturbances of circulatory function are poorly understood, and present

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methods of treatment leave much to be desired. Most of the studies have been primarily concerned with blood pressures. Such observations as have been made on the cardiac output have been carried out in most instances by plethysmographic methods, which in themselves tend to produce shock and hence are relatively valueless for the purpose. Aub and Cunningham,¹ however, using the Fick method, found a marked reduction in cardiac output, as well as a reduction in blood pressure, in experimental traumatic shock. Blalock and Harrison² observed a similar reduction in cardiac output after hemorrhage, but did not determine blood pressures.

The purposes of the present series of investigation have been (1) to attempt a determination of the relative importance of failure of the several circulatory functions in the more common and important types of shock, under conditions approximating clinical states as closely as possible, and (2) to attempt an evaluation of the various methods of treatment on the basis of these functional disturbances.

Shock produced by hemorrhage has been studied first, because of its clinical importance, and because it is almost the only type of shock for which there is a specific treatment (transfusion), against which various other therapeutic measures can be evaluated.

METHOD

Dogs of various sizes were used. Morphine was employed as an anesthetic. Although this drug may cause changes in cardiac output, as Tappan and Torrey³ have shown, the change is less marked than that produced by urethane (Tappan and Torrey), ether (Blalock⁴) or chloroform (Blalock⁵), and is less inconstant than that produced by barbital (Harrison, Wilson and Pilcher⁶). Furthermore, the minute cardiac output of the morphinized dog is not altered by changes in rate dependent on variations in vagal tone (Tappan and Torrey), and in this respect it is similar to the minute cardiac output of the trained unnar-

1 Aub, J. C., and Cunningham, T. D. Studies in Experimental Traumatic Shock—Oxygen Content of the Blood, *Am J Physiol* **54** 408, 1920.

2 Blalock, A., and Harrison, T. R. The Regulation of Circulation. V. The Effect of Anemia and Hemorrhage on the Cardiac Output of Dogs, *Am J Physiol* **80** 157, 1927.

3 Tappan, V., and Torrey, E. H. Studies on the Cardiac Output of the Dog. III. Influence of Pulse Rate upon Minute Volume Under Anesthesia, *Am J Physiol* **78** 376, 1926.

4 Blalock, A. Cardiac Output in the Dog During Ether Anesthesia, *Arch Surg* **14** 732 (March) 1927.

5 Blalock, A. The Effects of Ether, Chloroform and Ethyl Chloride Anesthetics on the Cardiac Output and Blood Pressure, *Surg Gynec Obst*, to be published.

6 Harrison, T. R., Wilson, C. P., and Pilcher, C. Personal communication to the author.

cotized dog (Marshall⁷) Finally, the cardiac output of the morphinized dog may be constant for a period of hours (Harrison and Leonard⁸) after an initial decrease within the first two hours (Tappan and Torrey)

Although morphine has seemed to be the least undesirable anesthetic for the purpose, there are some objections to its use, as it causes slowing of the pulse and may alter the response of the circulation to various abnormal states (Harrison, Wilson and Blalock,⁹ Marshall¹⁰) For this reason a few experiments have been done on trained unnarcotized animals

The dogs were given the drug (from 4 to 6 mg per kilogram of body weight) from two to six hours before the start of the experiment The mean blood pressure was measured by a cannula in the femoral artery The oxygen consumption was determined with the Benedict spirometer, the Roth graphic recording device being used Samples of blood were drawn from the right and left ventricles, with the usual precautions against contamination with air, and analyzed in duplicate for oxygen content in the Van Slyke-Neill manometric blood gas apparatus (some of the samples of arterial blood were obtained from the femoral artery) The cardiac output was calculated from the Fick formula

$\frac{\text{Cc oxygen consumed per minute}}{\text{Cc oxygen taken up by cc of blood in passing through the lungs}} = \text{Cc of blood passing through the lungs per minute}$

(It should be emphasized that the animals were not subjected to any operative procedure other than the insertion of an arterial cannula and repeated punctures of the heart The absence of manipulative shock is believed to be important in the proper study of hemorrhagic shock)

After one or more control determinations of cardiac output, the animal was bled from the femoral artery The amount of blood withdrawn varied in different experiments In many instances several determinations of minute cardiac output were made after several successive bleedings In most of the experiments a sufficient number of observations was made to allow the drawing of definite conclusions as to whether the fall in blood pressure occurred before or after the fall in minute cardiac output

When a typical state of shock—with tachycardia, diminished mean blood pressure and decreased cardiac output—had been reached, a therapeutic procedure was instituted, and its effect on pulse rate, mean blood pressure and minute cardiac output was then determined It was considered unwise to use two or more methods of treatment at the same time, as the evaluation of their relative importance would have then been difficult The following therapeutic measures were employed in various experiments

A Transfusion—In seven experiments sodium citrate was added to the blood which was removed, and transfusion into the femoral vein was carried out after

7 Marshall, E K, Jr Studies on the Cardiac Output of the Dog I The Cardiac Output of the Normal Unanesthetized Dog, *Am J Physiol* 77 459, 1926

8 Harrison, T R, and Leonard, B W The Action of Digitalis on the Cardiac Output of Dogs, *J Clin Investigation* 3 1, 1926

9 Harrison, T R, Wilson, C P, and Blalock, A The Effects of Changes in Hydrogen Ion Concentration on the Blood Flow of Morphinized Dogs, *J Clin Investigation* 1 547, 1925

10 Marshall, E K, Jr Studies on the Cardiac Output of the Dog, Influence of Atropin and Carbon Dioxide on the Circulation of the Unanesthetized Dog, *J Pharmacol & Exper Therap* 29-167, 1926

the state of shock had been induced. The transfusion was usually done in several stages, the animal being studied after various fractions of the withdrawn blood had been restored. (Seven experiments were performed, including forty-eight determinations of cardiac output.)

B Drugs—The drugs used were as follows

1 Digitalis was administered—from 0.25 to 0.5 cc per kilogram intravenously. The minute cardiac output was determined at intervals of from twenty minutes to two hours after the drug was administered. (Five experiments were performed, including fifteen determinations of minute cardiac output.)

2 Strychnine was administered as strychnine sulphate—from 0.5 to 0.8 mg per kilogram—intravenously or subcutaneously. The minute cardiac output was determined from six to twenty-five minutes after intravenous administration, and from fifteen minutes to one hour after the subcutaneous administration of the drug. (Five experiments were performed, including fifteen determinations of minute cardiac output.)

3 Ether was used, because I¹¹ have demonstrated that ether anesthesia causes an increased minute cardiac output in normal dogs and morphinized dogs. Ether was administered in doses of from 0.14 to 0.23 cc per kilogram, intramuscularly in three experiments and intra-arterially in five experiments. The latter method was used because Ranson, Windle and Faubion¹¹ found that intra-arterial injections of ether were safer than intramuscular injections. Blood samples were drawn from five to twenty minutes after the drug had been given. In several instances a rapid intravenous injection of ether was followed by immediate death of the animal, this occurring before observation on the circulation could be made. (Eight experiments were performed including twenty-three determinations of cardiac output.)

4 Caffeine was administered as caffeine sodium benzoate in doses of from 4 to 65 mg per kilogram. The determinations of cardiac output were made at various intervals—from three to forty minutes after intravenous doses, and from seven to forty minutes after subcutaneous doses. (Eight experiments were performed, including twenty-nine determinations of cardiac output.)

5 Epinephrine hydrochloride was given intravenously or subcutaneously—from 0.05 to 0.18 mg per kilogram. The circulatory measurements were carried out at time intervals of from two to forty-five minutes after the administration of the drug. (Seven experiments were performed, including twenty-three determinations of cardiac output.)

6 Ephedrine was administered as the hydrochloride. The drug was given subcutaneously, the dose being 2 mg per kilogram. (Three experiments were performed, including fourteen determinations of cardiac output.)

C Saline Infusion—Physiologic sodium chloride solution was administered intravenously in seven experiments. The total amount administered varied from 13 to 40 cc per kilogram. The observations were made at various time intervals—from four minutes to five hours—in the different experiments after the infusion. (Seven experiments were performed, including eighteen determinations of cardiac output.)

¹¹ Ranson, S. W., Windle, W. F., and Faubion, L. R. Vasodilator Mechanisms. V. The Intra-Arterial Injection of Ether, *Am J Physiol* 64:320, 1923.

RESULTS

As the results in the morphinized animals and the trained animals were similar, the two groups are presented together.

The Effects of Bleeding (tables 1 and 2, charts 1, 2, 3 and 11) — The different animals varied in the degree of resistance to hemorrhage

TABLE 1—*Effects of Hemorrhage on Circulation*

Ex- peri- ment	Weight, kg	Pulse Rate	Before Bleeding			After Bleeding					
			Oxygen Con- sump- tion per Minute, Cc	Mean Blood Pres- sure, Mm Mercury	Car- diac Output per Minute, Cc	Time After Last Bleed- ing, Minutes	Total Amount Bled, Cc. per kg	Pulse Rate	Oxygen Con- sump- tion per Minute, Cc	Mean Blood Pres- sure, Mm Mercury	Car- diac Output per Minute, Cc
1	16	50	136.8	120	2,330	35	13	120	117.6	110	1,890
2	19	80	151.1	112	2,520	20	14	180	121.2	100	1,210
		84	167.4	116	2,460	5	21	152	150.2	118	1,800
3	13.7	64	82.3	106	2,080	20	21	176	140.2	116	1,460
						60	20	40	83.0	96	1,910
						10	30	92	87.8	101	1,020
4	18	100	140.1	124	4,250	120	30	192	95.7	93	1,170
						1	22	115	165.6	114	2,460
						120	22	150	158.1	120	1,180
						1	32	195	158.1	88	1,886
5	8.5	54	79.2	98	1,240	40	32	180	165.6	72	1,410
						85	32	195	180.0	78	1,600
						5	23	180	81.6	88	930
						25	23	176	101.4	88	1,060
6	15	54	136.8	122	2,480	63	23	175	72.0	97	720
						5	15	200	50.1	76	890
						18	15	200	37.8	18	970
						1	23	120	111.0	118	2,500
7	11.8	56	90.0	108	1,970	19	23	125	110.4	125	1,020
						3	30	180	111.0	101	1,210
						35	30	200	108.0	70	830
						3	20	68	91.8	105	1,590
8	17	64	101.2	127	2,610	31	20	66	93.6	96	1,110
						4	39	150	100.8	70	1,200
						23	39	150	86.1	79	910
						15	20	84	127.0	122	1,770
						10	20	100	115.6	126	2,270
9*	10	90	117.0	106	2,710	5	30	92	131.3	118	1,710
						40	30	190	150.0	118	2,030
						10	40	230	150.0	102	1,300
						25	27	95	109.8	99	1,310
10*	11	88	109.2	119	2,350	20	37	180	100.8	79	1,150
						25	47	150	102.6	40	860
						20	12	150	118.1	92	1,620
11	9.5	88	96.9	130	2,020	65	12	168	99.0	108	1,190
						70	22	192	100.2	76	1,210
						16	21	88	85.6	121	1,310
						76	21	92	85.5	119	1,210
12	11	88	109.2	119	2,350	1	21	118	89.3	118	1,260
						1	27	185	91.2	107	1,100
						1	30	205	93.1	112	1,020
						1	33	200	91.2	92	800
						80	35	200	87.4	50	700

* Trained unnaeotized dog

Ordinarily, bleeding up to 15 cc per kilogram did not cause any striking change in the general condition. Evidence of shock, as manifested by tachycardia and slight stupor, was first noted when from 20 to 30 cc of blood per kilogram had been removed. The withdrawal of amounts greater than 40 cc per kilogram was usually followed by death.

in a relatively short time. The animals could survive greater loss of blood when they were bled slowly than when the hemorrhage was rapid. They tended to recover rapidly from mild shock, but severe shock once induced was usually progressive and fatal, even if no further bleeding was done.

The pulse rate was increased. Respiratory cardiac arrhythmias disappeared. The breathing was usually not altered until shock became extreme, when rapid and shallow breathing sometimes occurred. The arterial oxygen content was diminished, but not in great degree in most experiments, the usual change being from 1 to 3 per cent by volume corresponding to a diminution in hemoglobin of from 5 to 15 per cent. These results are in general similar to those of Blalock and Harrison² in their observations on hemorrhage.

The consumption of oxygen was often slightly increased after the initial bleedings, but was diminished in the more severe stages of shock.

The mean blood pressure was not significantly diminished until relatively large amounts of blood had been withdrawn. During and at the conclusion of a small bleeding the pressure was sometimes slightly below normal, but a rapid return to the normal level was the rule. (In considering changes in blood pressure, cardiac output and pulse rate, all values within 10 per cent of that during the control period have been considered as within the normal limits.) Of twenty-eight observations on animals which had been bled between 20 and 30 cc per kilogram, the mean blood pressure was normal in twenty, nineteen measurements on animals which had been bled more than 30 cc and less than 40 cc per kilogram, the mean pressure was reduced in fifteen. In every instance in which more than 40 cc of blood per kilogram had been withdrawn, the mean pressure was reduced. When the mean pressure once started to diminish, a rapid decline was the rule, even though the succeeding bleedings were of small magnitude. A dog weighing 10 Kg which had exhibited a decline of only 10 mm of mercury after being bled 300 cc might show a diminution of an additional 40 mm, after losing an additional 30 cc of blood. These observations are in accord with Porters¹² conception of a "critical level of blood pressure," and indicate that 30 cc per kilogram is, for most dogs, approximately the "critical" amount of blood which can be lost without consequent severe shock.

Tachycardia always preceded the fall in blood pressure. The relative stability of the blood pressure despite large hemorrhage was one of the most striking features of the experiments.

The minute cardiac output was always diminished after hemorrhage. The degree of diminution was well beyond the limits of error of the

¹² Porter, W. T. Traumatic Shock from Fat Embolism of the Vasomotor Center, *Am J Physiol* **71** 277, 1925.

method (from 5 to 8 per cent) in every instance except two. Loss of from 15 to 20 cc of blood per kilogram was regularly followed by decreased minute cardiac output, a loss of 30 cc per kilogram was usually necessary to produce a drop in mean blood pressure. Diminution in the mean blood pressure did not precede the decline in cardiac output in any experiment, the reverse was always the case. The minute cardiac output was usually diminished by more than one-third, and often by more than one-half, before a significant (greater than 10 per cent) decline in mean blood pressure occurred.

Ordinarily, the diminution in minute cardiac output was associated with an increase in pulse rate, the stroke output being, therefore, greatly diminished. In those experiments in which repeated observations were made during small successive bleedings, it was found that the minute cardiac output diminished before the pulse rate increased significantly. This relationship was noted in four experiments, whereas the change in pulse rate preceded the change in minute output in only one experiment.

The temporal relationships between the three circulatory factors is well illustrated in charts 1, 2, 3 and 11. As can be seen, the first striking change with hemorrhage is the diminution in minute cardiac output. The second change is in the pulse rate, which increases. The fall in mean blood pressure occurs last.

The Effects of Various Therapeutic Measures—Transfusion. The results of this procedure are presented first for the sake of comparison with the other forms of treatment, and are shown in table 2 and chart 3. When the degree of shock was not extreme, the animal could be readily restored to a relatively normal condition by the infusion of from one half to two thirds of the amount of blood which had been withdrawn. The results of transfusion, even if all the blood was replaced, were considerably less satisfactory in those animals which had reached a state of severe shock. In such instances, transfusion produced temporary improvement, but the animal often died from one to two hours later.

The consumption of oxygen was usually increased above the shock level and often above the original control level. This indicates that an oxygen debt may be present in shock, this will be discussed later.

The pulse rate did not return to normal after transfusion in any experiment. Only a slight degree of slowing was produced. The usual pulse rates were from 180 to 220 before transfusion and from 160 to 200 after transfusion.

The mean blood pressure was increased above the preceding level by the administration of blood, but usually did not reach the normal value for the animal. After a small transfusion, the rise was poorly sustained and was followed by a secondary decline, but when larger amounts of blood were given the pressure remained above the shock level, except

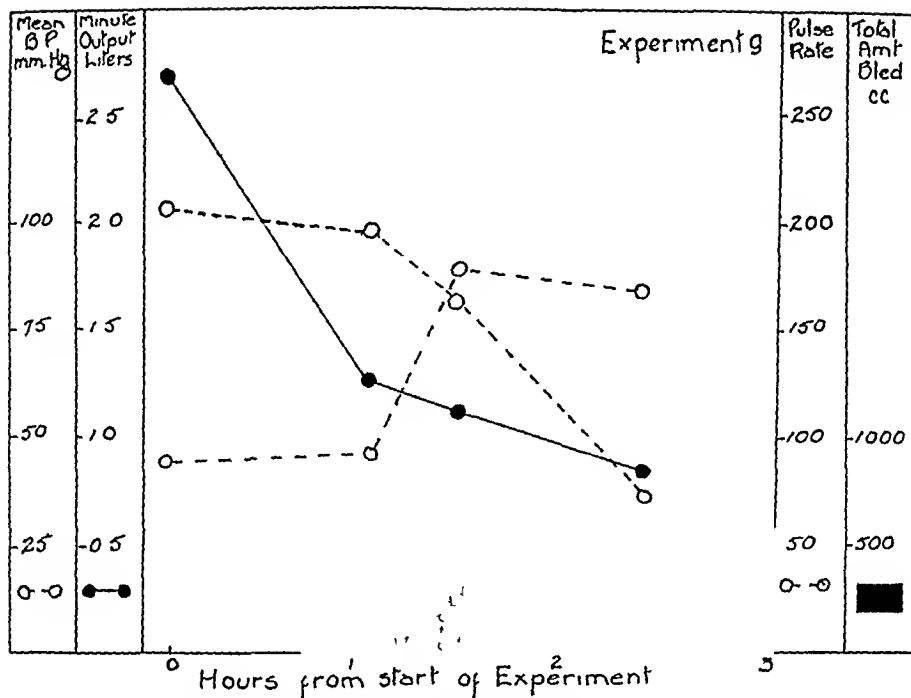


Chart 1—Effects of hemorrhage on circulation in a trained unnarcotized dog First the minute cardiac output diminished, then the pulse rate increased and finally the blood pressure decreased The animal was not given any general anesthetic or narcotic and had previously been trained to the method

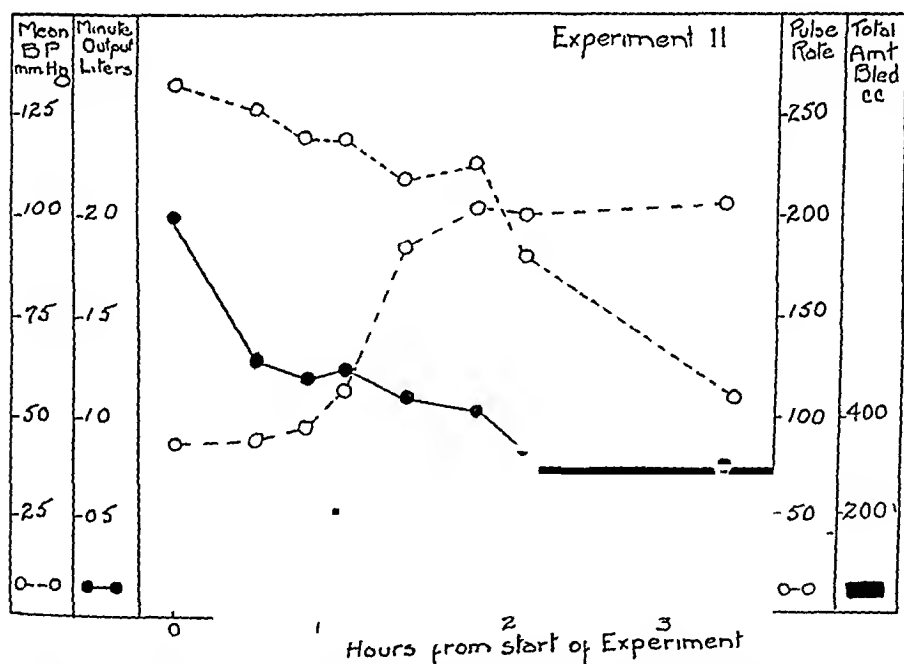


Chart 2—Effects of hemorrhage on circulation in a morphinized dog The usual temporal relationships are shown, the minute output decreasing first, the pulse rate increasing next and the mean blood pressure not showing any striking decline until the minute output was more than 50 per cent below normal

TABLE 2—Effect of Bleeding and Transfusion on Circulation of Dogs

Ex- per- iment	Before Bleeding				After Bleeding			Before Transfusion				After Transfusion						
	Weight, kg	Pulse Rate	Oxygen Consump- tion per Minute, Cc	Mean Blood Pressure, Mm Mercury	Cardiac Output per Minute, Cc	Time After Last Bleed- ing, Minutes	Total Amount Bled, Cc	Pulse Rate	Oxygen Consump- tion per Minute, Cc	Mean Blood Pres- sure, Mm Mercury	Cardiac Output per Minute, Cc	Time After Trans- fusion, Minutes	Total Amount Trans- fused, Cc per Kg	Pulse Rate	Oxygen Consump- tion per Minute, Cc	Mean Blood Pres- sure, Mm Mercury	Cardiac Output per Minute, Cc	
12	7	60	69.5	88	1,180	10	25	210	54.0	98	960	7	17	160	60.1	95	1,150	
						5	31	204	31.8	15	600	5	22	180	13.9	66	800	
13	10	48	73.1	83	2,160	10	13	76	70.3	85	1,070	15	12	118	62.9	54	970	
						5	23	210	68.5	12	690	20	22	108	66.6	73	1,140	
14*	11			108		12	15	155	111.0	50	1,090	1	8	180	152.0	70	2,080	
						20	15	180	111.0	18	1,130	1	18	180	163.1	71	2,960	
												1	16	180	159.6	86	1,030	
												15	15	180	169.6	98	3,800	
15*	11	88	109.2	119	2,350	70	20	192	100.2	76	1,210	20	10	210	107.3	71	1,100	
						165	20	220	109.1	52	1,140	60	10	215	77.7	18	800	
16	16	60	138.6	94	2,280	15	51	220	133.2	66	1,220	20	25	160	140.1	97	2,160	
						35	64	230	129.6	69	1,130							
						120	64	250+	179.2	14	1,160	15	62	180	215.8	111	3,520	
17	13.2	68	112.2	111	2,770	30	30	200	92.2	28	1,400	10	16	168	101.1	70	2,640	
		68	109.6	116	2,910							35	16	176	95.7	77	1,120	
												65	16	200	109.9	77	1,630	
18	10	70	86.7	102	1,810	20	30	78	71.3	102	940							
		72	83.1	105	1,750	15	33	84	73.6	101	970							
						20	37	120	76.0	106	860							
						20	40	160	80.8	103	870							
						20	44	180	90.3	96	770							
						70	47	190	86.9	14	610							
												1	12	180	102.1	70	870	
												1	21	180	122.3	90	1,400	
												1	32	180	111.0	64	1,620	
												1	35	180	110.1	68	1,700	
												40	35	180	109.3	76	1,300	
												110	35	200	101.1	80	1,670	
												185	35	190	103.3	77	1,510	

* Trained unanesthetized dog

in those instances in which the dog was moribund before transfusion was instituted. In several experiments, the infusion of blood was begun when the animal was dying from respiratory failure, but beneficial effects were not achieved, even when artificial respiration was also administered.

The minute cardiac output was increased in every instance. The degree of increase was directly proportional to the amount of blood replaced and inversely proportional to the degree of shock. Twenty-two determinations of cardiac output were made after transfusion. In eleven of these, the minute output was below the original normal value, in eight instances an approximately normal level had been reached,

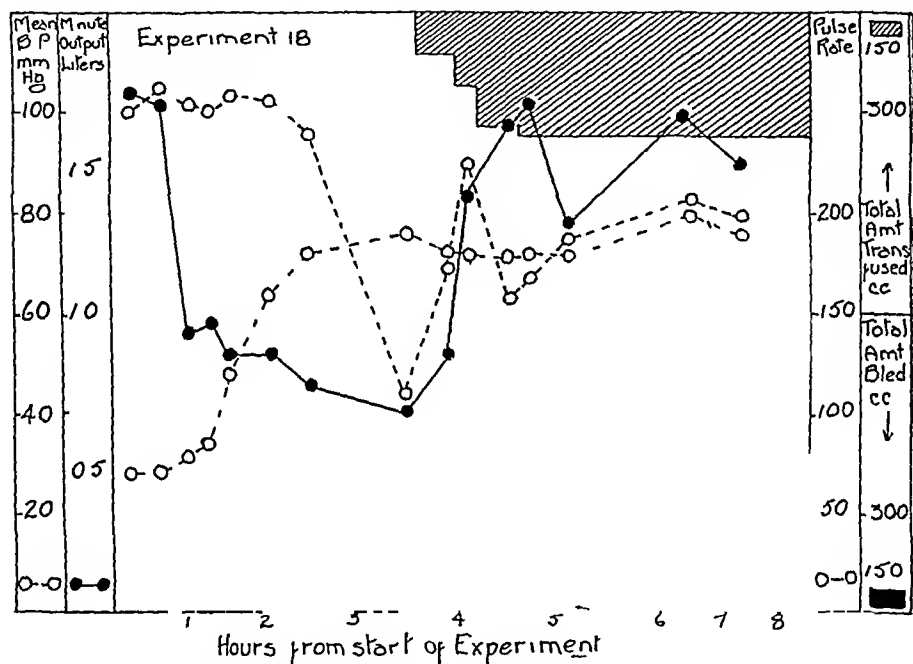


Chart 3—Effects of hemorrhage and transfusion on circulation. The usual effects of successive bleedings are shown. Transfusion caused the blood pressure to rise first. The minute output returned to above the normal level after all the blood withdrawn had been replaced. Transfusion had practically no effect on the pulse rate.

whereas in three the minute output after transfusion was greater than that before bleeding. The stroke output was always increased by transfusion, but it did not approach the normal value because the pulse rate remained rapid.

The effect of transfusion on minute cardiac output was usually permanent if the animal had been in a mild state of shock, but always temporary if the condition was poor before blood was replaced. In the latter instances, the minute output tended to diminish following the immediate rise after transfusion. When the amount of blood restored

TABLE 3—Effect of Digitalis on Circulation of Dogs in State of Shock Produced by Hemorrhage

Experiment	Weight, Kg	Before Digitalis					After Digitalis						
		Time After Bleeding, Minutes	Total Amount Bled, Cc per Kg	Pulse Rate	Oxygen Consumption per Minute, Cc	Mean Blood Pressure, Mm Mercury	Cardiac Output per Minute, Cc	Time After Drug, Minutes	Total Amount of Drug Given, Mg per Kg	Pulse Rate	Oxygen Consumption per Minute, Cc	Mean Blood Pressure, Mm Mercury	Cardiac Output per Minute, Cc
20	5.7	120	42	160	73.8	80	820	17	53	114	61.8	80	600
21	10	35	22	200	121.6	70	1,180	35	28	100	125.1	58	1,070
								70	28	200	125.1	43	990
								105	28	210	129.2	36	1,070
22	13	30	10	160	129.2	85	1,160	20	31	200	121.6	75	1,430
23	11	120	40	160	87.1	30	680	8	37	185	106.1	42	820
								21	37	195	77.9	32	600
24*	9	60	39	180	87.4	54	1,000	20	44	190	72.2	48	600
								25	44	190	72.2	48	570

* Trained unanesthetized dog.

approached the amount withdrawn, the minute cardiac output usually remained at an approximately normal level. After smaller transfusions there was an initial rise and then a fall in the minute output, which, however, remained above the pretransfusion level.

In general, the effect of the restoration of blood was more marked on the minute cardiac output than on the blood pressure. In this respect transfusion and bleeding were similar.

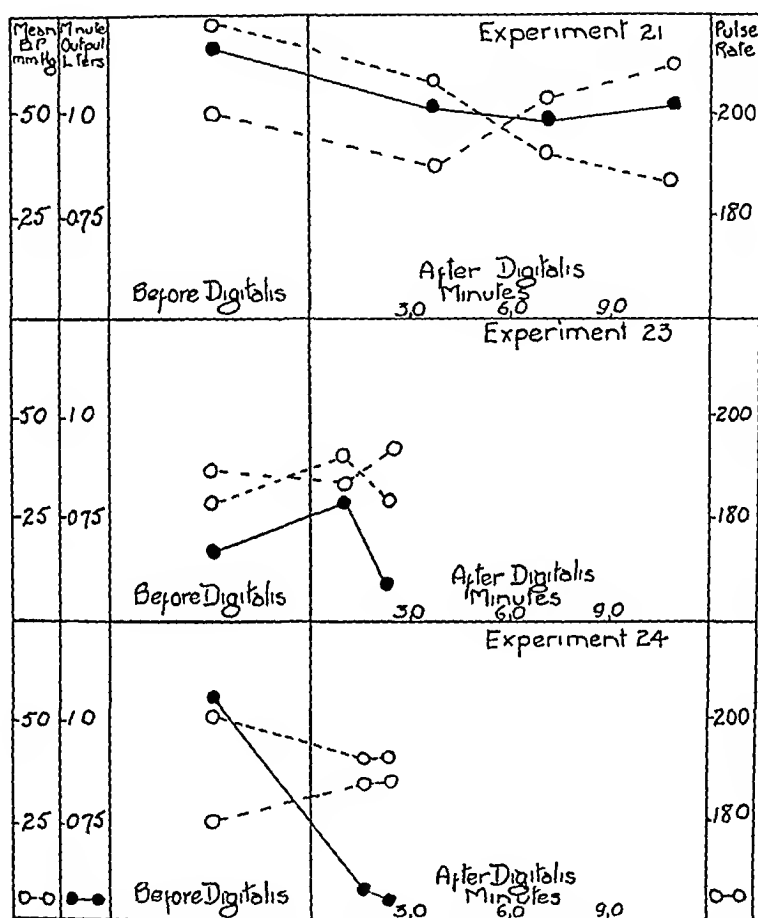


Chart 4—Effect of digitalis on circulation of dogs in a state of hemorrhagic shock. Digitalis caused a diminished minute output in each instance. In one of the three experiments there was a slight initial rise in this function. The blood pressure was not increased by the drug and practically no effect on pulse rate was observed.

The effects of removing and replacing blood on the circulation may be summarized as follows. Repeated bleeding causes a diminution in cardiac output, followed by an increase in pulse rate, which is succeeded by a fall in mean blood pressure. Transfusion causes each of these factors to return toward normal, but the effect is greatest on the cardiac output and least on the pulse rate, the blood pressure being intermediate.

TABLE 4—*Effect of Strychnine on Circulation of Dogs in State of Shock Produced by Hemorrhage*

Experiment	Weight, Kg.	Before Strychnine					After Strychnine					Method of Administration		
		Time After Bleeding, Minutes	Total Amount Bled, Cc per Kg.	Pulse Rate	Oxygen Consumption per Minute, Cc	Mean Blood Pressure, Mm. Mercury	Cardiac Output per Minute, Cc	Time After Giving of Drug, Minutes	Total Amount of Drug Given, Mg per Kg.	Pulse Rate	Oxygen Consumption per Minute, Cc		Mean Blood Pressure, Mm. Mercury	Cardiac Output per Minute, Cc
25*	8	30	25	180	50.4	35	630	35	5	210	16.8	40	100	Intramuscular
26	12	20	30	135	122.1	60	1,680	6	5	160	97.2	63	1,160	Intravenous
27	13	20	35	175	119.6	77	1,530	16	3	180	125.1	73	1,170	Subcutaneous
								76	3	190	129.2	81	1,160	
28	11	60	10	150	93.1	104	1,000	15	4	75	98.8	104	1,110	Subcutaneous
								37	4	80	117.8	101	1,100	
29*	11	180	28	180	106.7	60	1,290	7	4	200	110.6	58	1,380	Subcutaneous
								23	4	210	115.7	60	1,320	
								55	4	210	115.7	55	1,420	

* Trained unnaeotized dog

Drugs 1 Digitalis Inspection of table 3 and chart 4 demonstrates that digitalis when given in "therapeutic" amounts is harmful in shock.

The pulse rate was diminished in one instance and unchanged in eight observations after the drug was given. The mean blood pressure was increased once, unchanged twice and diminished in six determinations. In one experiment the minute cardiac output showed an initial rise, followed by a fall. In the remaining experiments, the drug produced a diminution in minute cardiac output. The degree of decrease varied from 2 to 45 per cent, and was in general proportional to the amount of the drug given. These observations confirm the results of Harrison and Leonard,⁸ who observed diminished cardiac output after the use of digitalis in normal dogs, and who concluded that the drug

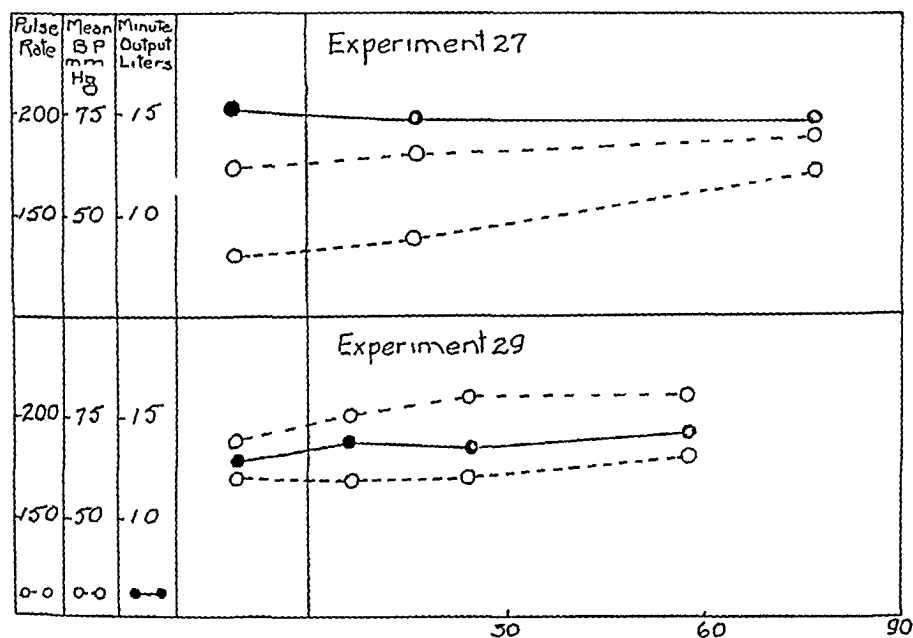


Chart 5—Two experiments showing that strychnine did not affect the circulation of dogs in a state of hemorrhagic shock

should not be given in shock. Of the several therapeutic measures which have been applied in this study, digitalis has been the most consistently harmful and has uniformly been without benefit.

2 Strychnine The results with this drug are shown in table 4 and chart 5.

No effect on the general condition of the animals was noted. The oxygen consumption was diminished in two instances and increased in seven observations. The pulse rate was diminished in one experiment and increased in the others. Significant alterations in mean blood pressure were not found. The minute cardiac output was decreased after the administration of strychnine in two experiments. In seven other observations, the minute cardiac output after strychnine was given was

TABLE 5—Effect of Injection of Ether on Circulation of Dogs in State of Shock Produced by Hemorrhage

Experiment	Weight, Kg	Before Ether					After Ether					Method of Administration		
		Time After Bleeding, Minutes	Total Amount Bled, Cc per Kg	Pulse Rate	Oxygen Consumption per Minute, Cc	Mean Blood Pressure, Mm Mercury	Cardiac Output per Minute, Cc	Time After Giving Drug, Minutes	Total Amount of Drug Given, Cc per Kg	Pulse Rate	Oxygen Consumption per Minute, Cc		Mean Blood Pressure, Mm Mercury	Cardiac Output per Minute, Cc
31	11	35	22	190	79.2	70	730	5	0.17	190	61.2	93	1,460	Intra-arterial
32	10	20	45	180	124.2	100	1,240	5	0.18	180	241.2	105	1,930	Intra arterial
33	11	210	27	200	118.8	47	1,570	2	0.14	205	122.4	66	1,460	Intra arterial
								10	0.14	210	122.4	71	1,330	
								22	0.14	210	104.4	63	1,110	
34	9	20	38	180	60.8		550	2	0.22	180	64.6	710	Intra arterial	
								7	0.22	190	49.4	430		
								18	0.22	200	51.3	410		
35	13	5 40	52 52	180 180	114.0 112.0	77 50	930 770	4	0.15	190	66.5	115	600	Intra arterial
								10	0.15	200	53.2	107	400	
								22	0.15	200	45.6	23	260	
36*	13	135	35	200	82.8	50	760	3	0.15	200	99.0	54	800	Intramuscular
37	14.8	40	27	160	100.8		1,150	6	0.23	175	102.6		1,260	Intramuscular
38	15	60	20	185	131.0		1,020	8	0.20	185	135.0		1,110	Intramuscular

* Trained unnaesthetized dog

within 10 per cent of the value before. These results are contrary to the observations on normal dogs of Wilson, Harrison and Pilcher,¹³ who found that strychnine produced increased minute output. The discrepancy between their results and those obtained in this study indicates that the action of the drug on normal animals is different from the effect on animals in a state of shock. In the latter, strychnine is either useless or harmful.

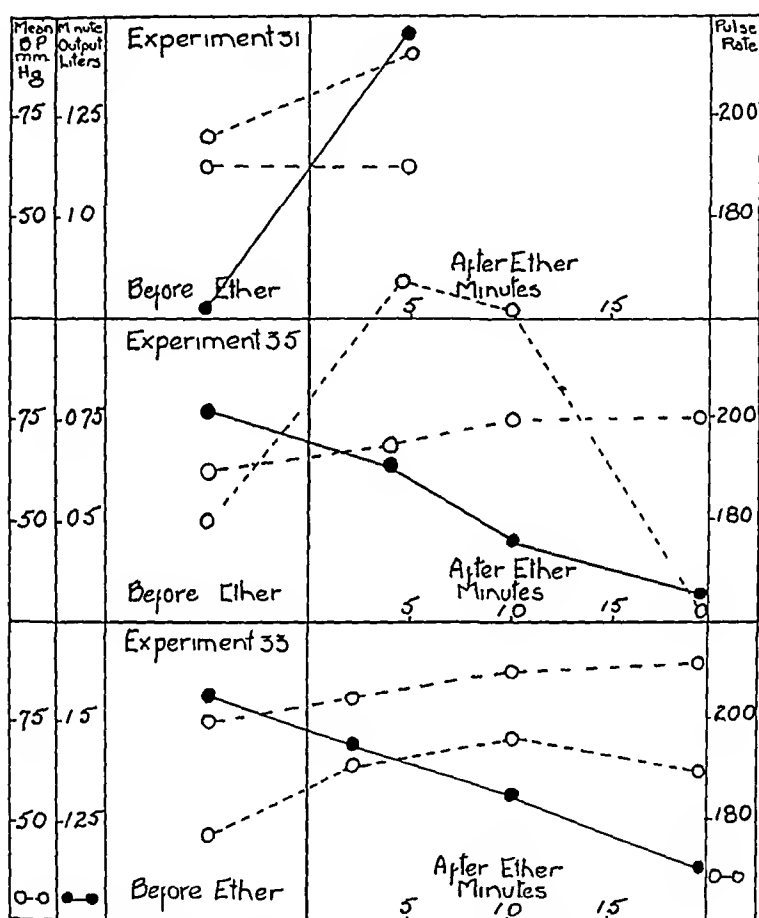


Chart 6—Effects of injection of ether on circulation of dogs in a state of hemorrhagic shock. The variability of the drug is shown. In each instance there was a temporary rise in blood pressure, but the cardiac output was markedly increased in one experiment and greatly diminished in two others.

3 Ether. In the use of this drug marked variability characterized the results, which are exhibited in table 5 and chart 6. When administered intramuscularly, ether did not cause any significant change in pulse rate or blood pressure and slight (less than 10 per cent) increase in minute cardiac output. When administered intravenously, ether caused the immediate death of the animal. After intra-arterial injections the

¹³ Wilson, C. P., Harrison, T. R., and Pilcher, C. P. To be published.

TABLE 6--Effect of Caffeine on Circulation of Dogs in State of Shock Produced by Hemorrhage

Experiment	Weight, Kg	Before Caffeine					After Caffeine					Method of Administration		
		Time After Bleed, Minutes	Total Amount Bled, Cc per Kg	Pulse Rate	Oxygen Consumption per Minute, Cc	Mean Blood Pressure, Mm Mercury	Cardiac Output per Minute, Cc	Time After Giving of Drug, Minutes	Total Amount of Drug, Mgr per Kg	Pulse Rate	Oxygen Consumption per Minute, Cc		Mean Blood Pressure, Mm Mercury	Cardiac Output per Minute, Cc
10	7.6	55	50	210	72.7		750	12	16	210	72.7		820	Intravenous
11*	7	40	34	150	73.8		720	7	17	150	97.2		1,010	Intravenous
12	7.2	60	38	130	63.0		630	20 5 10	25 93 93	150 180 200	73.1 71.6 72.0	750 770 580		Intravenous
13	5	25 25	32 11	170 190	41.1 54.0		530 520	12 5 23	22 41 44	120 100 195	57.6 50.4 39.0	700 470 350		Intravenous
14*	14	20 33	30 30	180 180	112.5 117.0	53 56	1,220 1,110	3 7 18 40 75	1 1 1 4 4	180 180 180 190 190	108.0 115.2 117.0 97.2 117.0	1,700 1,180 1,300 930 1,100		Intravenous
15	13.2	13 25	40 40	180 180	61.9 61.9	56 56	940 820	20 15	15 15	180 180	72.8 80.1	54 51	930 1,010	Subcutaneous
16	10.9	10	20	192	100.2	76	1,240	20 42	15 15	200 192	105.4 92.5	79 73	1,170 920	Subcutaneous
17	14	3	2	170	109.8	70	1,080	7	9	180	118.8	76	1,170	Subcutaneous

* Fasted unanesthetized dog.

pulse rate was unchanged or slightly increased, and the mean blood pressure was elevated. The minute cardiac output was strikingly elevated (100 per cent and plus 57 per cent) in two experiments. When beneficial effects on the cardiac output and blood pressure were obtained they came on within two minutes and were often followed within twenty minutes by depression. The observations on ether are in accord with the results previously published (Blalock⁴) concerning the effect of ether anesthesia on cardiac output. Increased minute output was found to occur during the early and usual stages of anesthesia, but prolonged ether narcosis caused a diminution in minute output.

4 Caffeine. The results with this drug are shown in table 6 and chart 7. In most of the experiments, the results were beneficial. The consumption of oxygen was often increased. The pulse rate was usually not altered. The mean blood pressure was increased in three observations, diminished once and unchanged in six instances, after administration of the drug. Of eighteen determinations after caffeine was given, the minute cardiac output was increased in nine, unchanged in six and diminished in three. Beneficial effects, when obtained, persisted for from thirty to sixty minutes. Harmful effects—diminution in minute output or mean pressure—occurred most often in those animals which were in a state of severe shock. In two experiments animals in severe shock died within a few minutes after being given caffeine. It was impossible to be certain whether the drug was the cause of death, although this seemed to be the case.

The results with caffeine, like those with strychnine, are contrary to the observations of Pilcher, Wilson and Harrison¹⁴ on normal dogs. These observers found that caffeine caused either no change or diminution in minute cardiac output. In this instance also, the drug affects the normal and abnormal circulation in opposite directions.

5 Epinephrine hydrochloride. The results, which are exhibited in table 7 and chart 8, were not constant. The pulse rate was diminished significantly in one experiment only, and usually was not altered. The mean blood pressure was increased immediately after the intravenous administration of epinephrine hydrochloride, but it usually fell within a few minutes to below the level reached before the drug was given. Subcutaneous doses of epinephrine hydrochloride did not cause a significant rise of pressure. The minute cardiac output was diminished in one experiment and increased in three instances after the intravenous administration of epinephrine hydrochloride. The rise was poorly sustained, and the minute output within ten or fifteen minutes after the administration was less than that before the drug was given. The subcutaneous administration of epinephrine hydrochloride caused a rise

14 Pilcher, C., Wilson, C. P., and Harrison, T. R. To be published

TABLE 7—Effect of Injection of *Epinephrine Hydrochloride* on Circulation of Dogs in State of Shock Produced by Hemorrhage

Experiment	Weight, Kg	Before <i>Epinephrine Hydrochloride</i>						After <i>Epinephrine Hydrochloride</i>						Method of Administration
		Time After Bleeding, Minutes	Total Amount Bled, Cc per Kg	Oxygen Consumption per Minute, Cc	Mean Blood Pressure, Mm Mercury	Cardiac Output per Minute, Cc	Pulse Rate	Time After Giving of Drug, Minutes	Total Amount of Drug Given, Mgr per Kg	Pulse Rate	Oxygen Consumption per Minute, Cc	Mean Blood Pressure, Mm Mercury	Cardiac Output per Minute, Cc	
50*	13	25	46	102.6	40	860	150	3	0.08	150	91.8	100	620	Intravenous
51	7.1	120	32	68.4	66	880	180	2	0.07	180	68.4	110	1,250	Intravenous
52	12.5	15	37	81.7	60	630	185	2	0.17	100	22.8	114	1,060	Intravenous
								6	0.17	120	43.7	88	2,110	
53	20	20	28	123.4	47	1,070	185	1	0.05	185	118.8	94	1,350	Intravenous
								5	0.05	185	137.0	34	1,220	
								10	0.05	185	109.0	34	920	
54	11	60	22	129.2	92	1,200	200	4	0.18	200+	129.2	90	1,300	Subcutaneous
								11	0.18	200+	125.4	56	1,200	
								30	0.18	200+	121.6	34	1,010	
55	13	15	30	102.6	80	1,170	90	7	0.15	120	137.8	90	2,090	Subcutaneous
								23	0.15	150	137.8	80	2,250	
								45	0.15	170	137.8	90	2,010	
56	13	50	29	66.6	50	550	215	5	0.09	215	63.0	40	400	Subcutaneous
								21	0.08	210	68.6	36	600	
								56	0.08	210	48.6	35	150	

* Trained unnaeotized dog

in minute output. This came within from five to ten minutes and lasted from twenty to forty-five minutes. When the degree of shock was not extreme, the benefit derived from epinephrine hydrochloride was of longer duration than in those experiments in which the animal was in a more critical condition.

These results are in accord with the observations of Odaira¹⁵ on normal rabbits, of Pilcher, Wilson and Harrison¹⁶ on normal dogs, and of Lyon and Sands¹⁷ on human subjects.

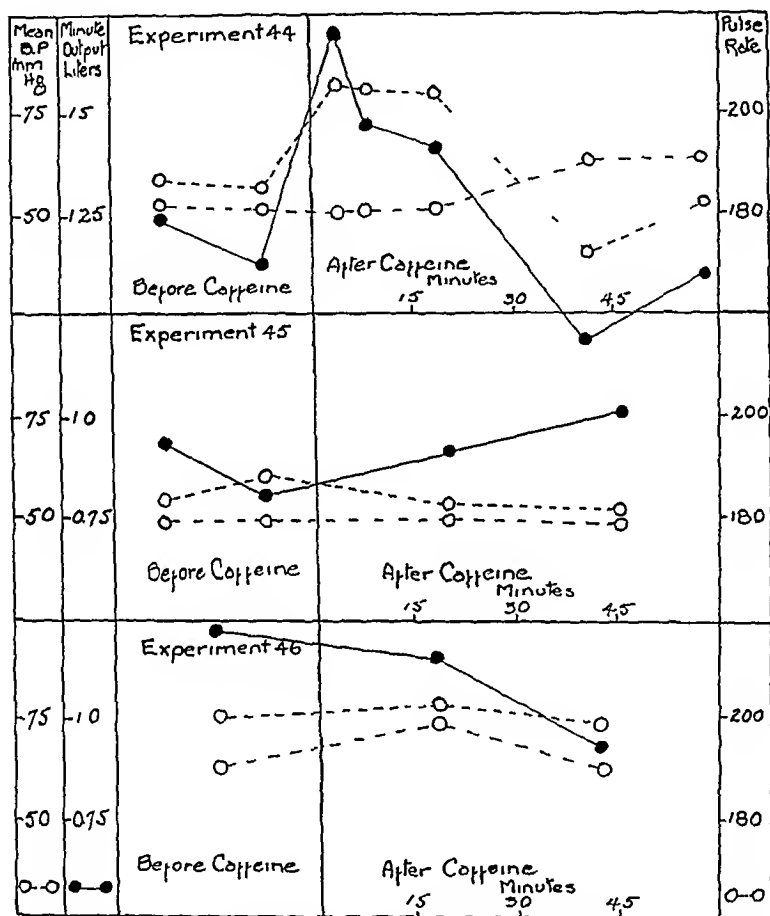


Chart 7—Effects of caffeine on circulation of dogs in a state of hemorrhagic shock. In one experiment it was beneficial, as shown by the increase in both minute output and blood pressure. In the second and third experiments, the drug had little effect. Harmful actions were not usually observed after caffeine.

6 Ephedrine. The results with this substance were on the whole more satisfactory than those with any of the other drugs investigated.

¹⁵ Odaira, T. Observations on Gaseous Metabolism and Minute Volume. I. Relation to Internal Secretions, *Tohoku J. Exper. Med.* **6**: 325, 1925.

¹⁶ Pilcher, C., Wilson, C. P., and Harrison, T. R. To be published.

¹⁷ Lyon, D. M., and Sands, J. Studies on Pulse Wave Velocity, Effect of Adrenalin, *Am. J. Physiol.* **71**: 534, 1925.

TABLE 8—Effect of Injection of Ephedrine on Circulation of Dogs in State of Shock Produced by Hemorrhage

In- ter- ment	Weight, Kg	Before Ephedrine					After Ephedrine					Method of Administration		
		Time After Bled- ing, Minutes	Total Amount Bled, Cc per kg	Pulse Rate	Oxygen Consump- tion per Minute, Cc	Mean Blood Pressure, Mm Mercury	Cardiac Output per Minute, Cc	Time After Giving Drug, Mins per Kg	Pulse Rate	Oxygen Consump- tion per Minute, Cc	Mean Blood Pressure, Mm Mercury		Cardiac Output per Minute, Cc	
57	13.2	30	27	176	95.7	77	1,420	20	2	230	146.2	80	2,200	Subcutaneous
		60	27	200	109.9	77	1,630	40	2	230	142.7	85	1,800	
								65	2	236	156.6	83	2,000	
								120	2	240	149.6	81	2,150	
58	10	25	40	230	129.6	69	1,130	15	2	180	147.6	66	1,230	Subcutaneous
								33	2	240	154.8	59	1,220	
								30	4	196	220.2	44	1,100	
								60	4	200+	179.2	41	1,100	
59*	11	123	20	192	92.5	73	920	20	2	163	114.7	79	1,120	Subcutaneous
								44	2	220	109.1	52	1,140	

* Trained unrecaptured dog.

They are shown in table 8 and chart 9. The consumption of oxygen was increased. The general condition of the animals seemed to be improved. The effects on pulse rate were inconstant. The mean blood pressure was slightly increased in five instances, slightly diminished twice and markedly diminished in three observations after the administration of the drug. The minute cardiac output increased each time after the drug was given and this rise was well sustained lasting for

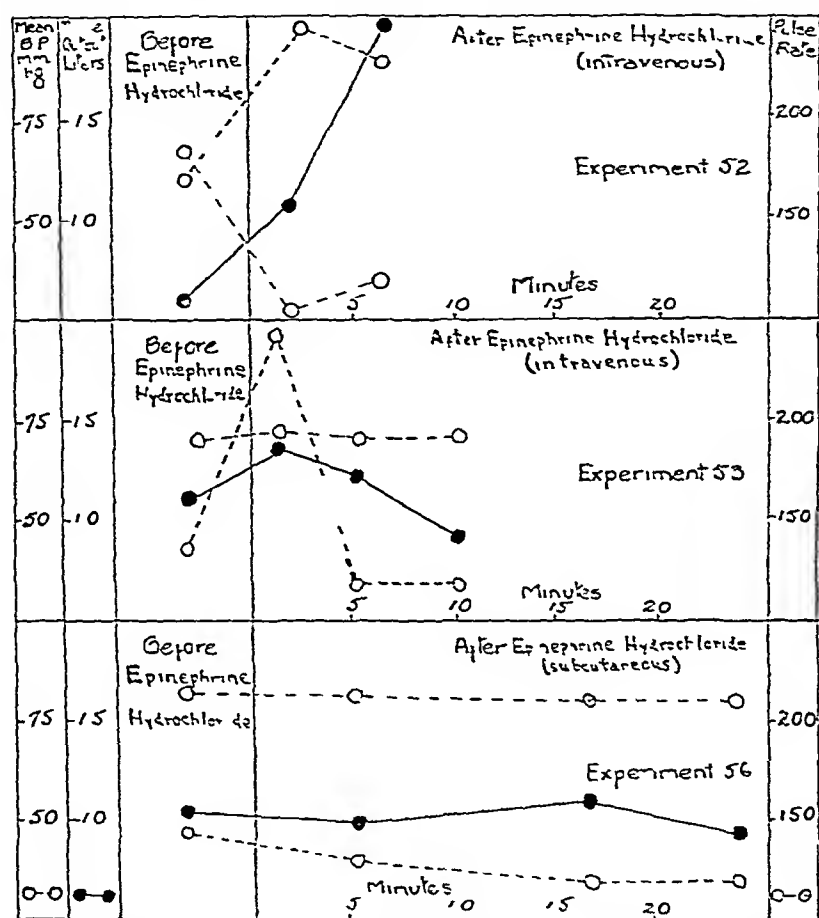


Chart 8—Effects of epinephrine hydrochloride on circulation of dogs in a state of hemorrhagic shock. It was very beneficial in one instance, slightly beneficial in a second and without effect in the third experiment. In experiment 52 the effect of the drug was not studied after the first ten minutes. The short duration of the beneficial effects in experiment 53 should be noted.

from one to two hours. When the shock state was not extreme the animal seemed to be greatly benefited. There was less benefit when the animal was in severe shock. In two instances moribund animals were given the drug. Both died before observations on the circulation could be made, and the impression was gained that the drug hastened their death.

TABLE 10—Effects of Hemorrhage on Maximum, Minimum and Mean Blood Pressure and Cardiac Output

Experiment	Weight, Kg	Before Bleeding					After Bleeding					Time After Last Bleeding, Minutes	Total Amount Bled, Ce per Kg		
		Pulse Rate	Oxygen Consumption per Minute, Ce	Maximum Blood Pressure, Mm Mercury	Minimum Blood Pressure, Mm Mercury	Mean Blood Pressure, Mm Mercury	Cardiac Output per Minute, Cc	Pulse Rate	Oxygen Consumption per Minute, Ce	Maximum Blood Pressure, Mm Mercury	Minimum Blood Pressure, Mm Mercury				
70	11.1	72	89	130	79	100	1,380								
		132	100	128	73	99	1,330	144	103	123	87	106	940	3	7
		132	107	119	74	94	1,260	220	98	108	76	90	680	25	12
71	12	62	78	160	54	95	1,860								
		60	74	166	53	94	1,600	56	75	114	75	105	1,640	15	10
		96	60	172	53	101	1,570	120	74	134	92	111	1,310	20	15
								200	87	130	97	114	1,020	20	20

As caffeine is probably more widely used clinically than any other drug in cases of shock, and since ephedrine seemed from this study to be the best of the various drugs studied, it was thought that a comparison of the action of these two substances might be of interest. The results of such an experiment performed on a trained unnarcotized animal are portrayed in chart 10. This dog had a normal minute cardiac output of 2,350 cc, and a normal mean blood pressure of 119 mm of mercury. After repeated bleedings the minute cardiac output was 1,240 cc and the mean pressure was 76. Caffeine was given subcutaneously. Twenty minutes after the drug was administered the output was 1,170 cc and the pressure 79. Forty minutes after caffeine was given the output was

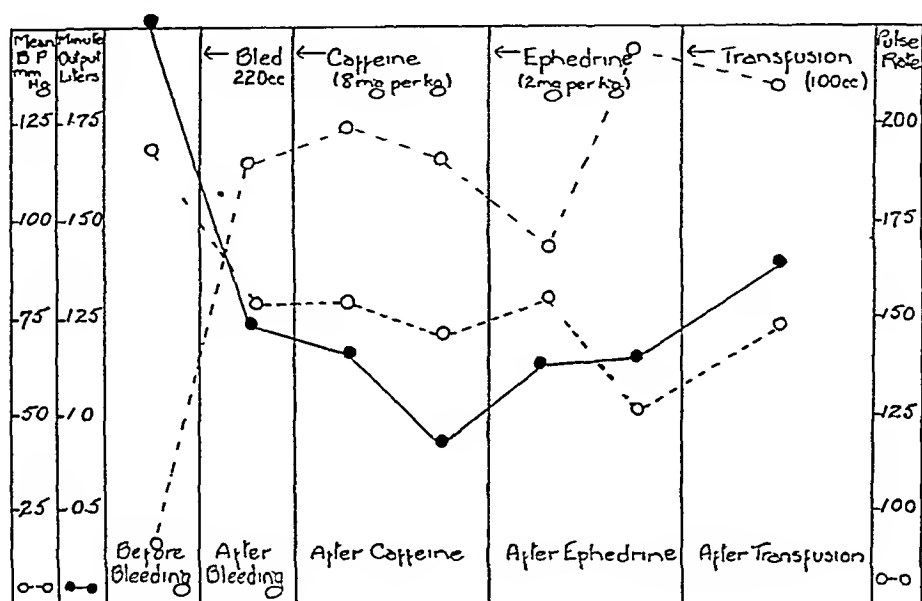


Chart 10—Comparison of effects of caffeine, ephedrine and transfusion on circulation of a dog in a state of hemorrhagic shock. In this experiment the minute output and blood pressure continued to diminish after the administration of caffeine. Ephedrine caused a lasting increase in minute output and a temporary increase in blood pressure. Transfusion had the usual effect (chart 4).

920 cc and the pressure 73. Ephedrine was administered. The pulse rate, which had not been altered by caffeine, decreased from 192 to 168. Twenty minutes after the administration of ephedrine the minute cardiac output had increased from 920 to 1,120 cc. Forty-five minutes after the drug was given the minute output was 1,140 cc. The mean blood pressure rose 6 mm and then dropped 20 mm. One hour after ephedrine had been given transfusion of 100 cc of blood was performed. Twenty minutes after transfusion the mean pressure had increased by 20 mm, and the minute cardiac output had increased from 1,140 to 1,400 cc. However, one hour after transfusion the minute

cardiac output had fallen to 800 cc, and the blood pressure to 48, the lowest level yet attained. Shortly after this, the dog died.

This animal was in a state of severe shock before any therapeutic measures were instituted. Despite (or possibly because of) the administration of caffeine, the minute output decreased. Ephedrine caused temporary improvement. Transfusion caused further temporary improvement, but the degree of the original shock was too great for the animal to be saved. This experiment seemed to demonstrate clearly the superiority of ephedrine over caffeine.

Saline Infusion The results are shown in table 9 and chart 11.

In every instance, the infusion of saline solution was followed by beneficial effects. The pulse rate was usually diminished. The mean

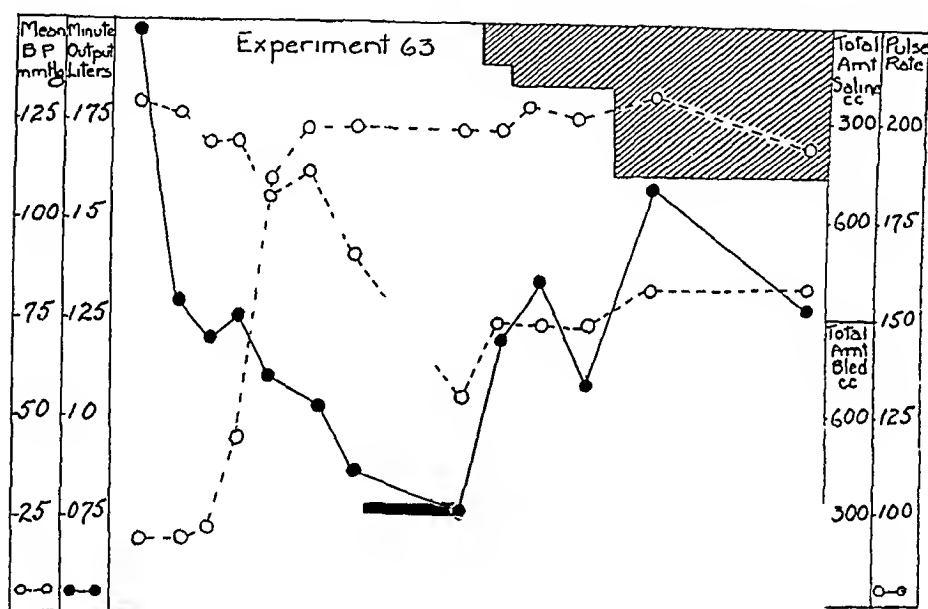


Chart 11—Effects of bleeding and saline infusion on circulation. Progressive hemorrhage caused the minute cardiac output to decrease. The pulse rate then increased, and finally the mean blood pressure diminished. After the first saline infusion a striking rise in minute output and a small rise in blood pressure occurred. The tendency of the blood pressure rise to be sustained and of the minute output to decline again after saline infusion are illustrated.

blood pressure was slightly decreased twice, and was increased in the other nine observations after the administration of saline solution. The minute cardiac output was increased in every instance, and the immediate rise was as great or greater than that produced by transfusion. The immediate benefits of saline solution were comparable to those from transfusion, but the results were less lasting, the animal tending to relapse into a state of shock within from one to three hours. The temporary and permanent effects of saline infusion were much better than those of any of the drugs investigated.

COMMENT

It is not practical to separate hemorrhage and shock completely in any consideration of the mechanism of their production. The two are usually seen together clinically and are often observed concurrently in laboratory animals. The present report contains only experiments on hemorrhage, and the following comment is limited to this specific type of shock so far as such a limitation seems consistent with clearness.

All investigators are agreed that the symptoms of shock following hemorrhage are primarily dependent on a diminished volume of blood. So far as the immediate condition is concerned, the loss of hemoglobin is in itself relatively unimportant.

At this point agreement ends. Concerning why and how loss of blood volume causes such profound disturbances of body function, there is no unanimity of opinion. There have been at least three opposing schools.

1 *Venopressor Mechanism*—Henderson and Harvey²⁰ showed that high carbon dioxide tension had little effect on arterial pressure, but caused a marked rise in venous pressure and, hence, they believed, in minute cardiac output. Conversely, low carbon dioxide tension caused a low venous pressure, which led to a diminution in the minute cardiac output and eventually to a low arterial pressure. According to this conception, carbon dioxide is to be regarded in the nature of a hormone which regulates venous pressure and, hence, indirectly affects cardiac output and arterial pressure. Low carbon dioxide tension was believed to be the result of overventilation and the cause of the circulatory collapse in shock.

A great many objections have been raised to this theory, and it is generally admitted to be no longer tenable. Overventilation and low carbon dioxide tension, when they occur, are now generally recognized as effects and not causes of shock.

2 *Diminished Arterial Pressure*—The prognostic value of arterial pressure in severe shock is universally admitted. The question is: Does a fall in arterial pressure antedate and initiate the other circulatory changes in shock? Apparently most observers believe so. The blood pressure is widely used both clinically and experimentally as a "guide" to the degree of shock. Wiggers²¹ recorded changes in arterial, intra-

²⁰ Henderson, Y., and Harvey, S. C. Shock and Acapnia, Veno-Pressor Mechanism, *Am J Physiol* **46** 533, 1918.

²¹ Wiggers, C. J. Shock Abdominal—Initial and Progressive Stages of Circulatory Failure in Abdominal Shock, *Am J Physiol* **45** 485, 1918, Shock and Circulatory Failure Following Trauma, *ibid* **46** 314, 1918, Differentiation Between Circulatory Failure Due to Shock and Other Causes, *J A M A* **70**: 508 (Feb 23) 1918.

ventricular and intra-auricular pressures by the optical method. He concluded that essentially the same circulatory mechanism prevailed in abdominal shock (exposure of intestines), traumatic shock and hemorrhage. In regard to the initial stages of abdominal shock,²² he said "As the contour of the intraventricular curves does not alter, as the heart rate, if it undergoes any change increases and as the pulmonary arterial pressure remains unaffected, the conclusion is reached that the reduction in blood content and fall in pressure in the arteries is not due to a decrease in the minute volume of the heart, but to a reduction in the total arterial resistance." Wiggers believed that the later and more significant fall in blood pressure was dependent on reduced minute cardiac output. Concerning hemorrhage, he wrote "Reduction of arterial resistance initiates the fall of arterial pressure, diminished venous return, a fall of effective venous pressure and a deficient cardiac discharge are prominent factors in the fatal fall of arterial pressure." Wiggers pointed out²³ that mean blood pressures might not adequately demonstrate the "distinct alteration" in "arterial pressure as recorded precisely." In my own experiments, mean blood pressure tracings have been used generally, and optical methods of registration have not been available. In order to meet Wigger's point, a few additional experiments have been done, and maximum and minimum pressures recorded. An example is shown in table 10.

These experiments show that the maximum pressure may fall and the minimum pressure may increase before there is a marked reduction in minute cardiac output. As the minimum pressure increases soon after bleeding, I cannot agree with Wiggers that the earliest changes in blood pressure are due to diminished peripheral resistance. The initial changes in blood pressure are to be considered as secondary to (1) compensatory vasoconstriction and (2) diminished output per beat. The minute output is usually diminished, but in those experiments in which tachycardia develops early the minute output may remain normal while the initial changes in blood pressure occur.

3 *Diminished Volume Flow of Blood*—Gesell²⁴ studied the blood flow through the salivary gland and the mean arterial pressure. He compared the effects of hemorrhage and shock resulting from tissue-abuse. As my conclusions reached from a study of the total circulatory minute volume are strikingly similar to his, based on observations of blood flow through a small portion of the body, I quote Gesell as follows:

22 Wiggers (footnote 21, first reference)

23 Wiggers (footnote 21, second reference)

24 Gesell, R. Studies on the Submaxillary Gland. IV. A Comparison of the Effects of Hemorrhage and Tissue-Abuse in Relation to Secondary Shock. *Am J Physiol* 47:468, 1918.

Volume flow of blood appeared to be the more fundamental problem, and, as the results will show, mean blood pressure gives very little evidence of the gravity of the disturbance. A primary rise in pressure occurring both in hemorrhage and tissue-abuse may be accompanied by a large decrease in volume flow of blood, constituting the greater part of the total decrease reached by a subsequent fall to zero pressure. It appears that too much weight is still given to the mean blood pressure, relative to the conditions obtaining. Here lies a danger of permitting the development of shock which might otherwise be avoided—similarity of the curves resulting from hemorrhage and tissue-abuse. It appears, therefore, that fundamentally the same factors controlling volume flow of blood are operating in the two conditions. All the experiments indicate the similarity of the vascular reactions in hemorrhage and tissue-abuse—the percentage decrease in volume flow of blood far exceeds the percentage decrease in blood volume in every experiment. The maintenance of a normal blood volume is, therefore, an extremely important function.

A reduction of volume flow amounting to 85 per cent of the initial flow may occur with a constant head of pressure or with a small change in head of pressure—a rise as well as a fall.

Gesell emphasized the importance of the “nutrient flow,” that is, the minute volume of flow multiplied by the percentage of red cells. He pointed out that the injection of an “inert” solution, although it caused a dilution of the blood and a diminished percentage of red blood cells was, nevertheless, of great benefit, because the degree of increase in volume following such injection was much greater than the degree of dilution. This he explained by Poiseuille’s law concerning the rate of flow of liquids through tubes. This rate of flow, other factors remaining constant, increases with the fourth power of the caliber of the tubes, whereas the degree of dilution increases only with the square of the caliber.

The similarity of the curves of basal flow in hemorrhage and tissue-abuse suggests similar vascular reactions of similar origin, a change in caliber of the vessels being the most important factor underlying the deflection of the curves.

Aub and Cunningham,¹ using the Fick method, found that the cardiac output might diminish before the blood pressure reached a shock level. In their experiment 56, the mean blood pressure was between 104 and 94 mm of mercury, whereas the oxygen content of the venous blood had fallen from 12.27 to 4.55 per cent by volume.

Cannon and Cattell,² in discussing the mechanism of shock, referred to Gesell’s work and suggested that whereas the blood flow through the peripheral organs might be reduced before the blood pressure diminished, the blood flow through the vital organs might be normal until the fall in

²⁵ Cannon, W. B., and Cattell, M. Studies in Experimental Traumatic Shock—Critical Level in a Falling Blood Pressure, *Arch. Surg.* 4:300 (March) 1922.

blood pressure occurred. However, Cannon²⁶ summarized the important physiologic abnormalities in shock and did not mention diminished minute cardiac output, which, from the work of Gesell, the studies of Aub and Cunningham and the results reported in this paper, seems to be the most important factor concerned, except the diminished blood volume.

My results are, in general, in rather close agreement with those of Gesell. He found somewhat greater reductions in volume in the flow of blood before the blood pressure began to diminish. It is to be expected, however, that the peripheral organs would show a relatively greater reduction in blood flow than would the total organism, for all compensatory mechanisms would act toward maintaining a normal or nearly normal flow in the more vital organs. This is in accord with the suggestion of Cannon and Cattell, previously mentioned.

The diminished oxygen consumption found in these experiments—also noted by Aub²⁷ and others—might conceivably be due to (1) a diminished oxygen requirement from impaired functional activity, or (2) an oxygen intake less than the oxygen requirement of the tissues due to the inability of the circulation to meet the demands of the body for oxygen. Hill and his collaborators²⁸ have distinguished between oxygen intake and oxygen requirement, and have shown that when the latter exceeds the former oxygen debt results. When an oxygen debt of any considerable magnitude occurs, lactic acid accumulates. The experiments of McLeod²⁹ indicated that the blood lactic acid is not significantly increased until shock becomes extreme.

The results of transfusion in my experiments indicate that both the factors mentioned previously may be effective in the diminished oxygen consumption during shock. The oxygen consumption after transfusion was usually greater than that immediately before this procedure. In some experiments it was less than the normal value for the animal and in some it was considerably greater than normal. In the former instances, that is, subnormal oxygen consumption after transfusion, it is logical to believe that the oxygen requirement during shock was diminished, whereas in the latter observations, that is, elevated oxygen consumption after transfusion, it seems evident that there was an actual oxygen debt during shock and that this was met by an increased oxygen consumption after transfusion.

²⁶ Cannon, W. B. Studies in Experimental Traumatic Shock, Evidence of a Toxic Factor in Wound Shock, *Arch. Surg.* **41** (Jan.) 1922.

²⁷ Aub, J. C. Studies in Experimental Traumatic Shock, Basal Metabolism, *Am. J. Physiol.* **54** 388, 1920.

²⁸ Hill, A. V., and Tupton, H. Muscular Exercise, Lactic Acid, and Supply and Utilization of Oxygen, *Quart. J. Med.* **16** 135, 1925.

²⁹ McLeod, J. J. R. Concentration of Lactic Acid in the Blood in Anoxemia and in Shock, *Am. J. Physiol.* **55** 184, 1921.

A great deal has been written about disturbances in acid base equilibrium in shock. At one time Henderson and Harvey²⁰ attributed the symptoms to acapnia (alkalosis from loss of carbon dioxide by over-ventilation), whereas Cannon³⁰ believed that acidosis was an important factor in shock (Cannon used acidosis to mean "diminished alkali reserve"). Wilson³¹ found an initial fall in blood bicarbonate, followed by a rise above normal and an alkalosis in experimental hemorrhage. More recently, Hertzman and Gesell have reported increased alkalinity of the arterial blood and increased acidity of the venous blood after hemorrhage. They attributed the arterial alkalosis to overventilation and the venous acidosis to a diminished volume of flow.

The disturbances in acid base balance during hemorrhage and probably also during shock apparently may be explained on the basis of the changes in minute blood flow. They are, in all probability, to be attributed in large measure to anoxemia dependent on diminished blood flow and consequent low tissue oxygen tension. In moderate degrees of shock with relatively slight impairment of medullary circulation, mild anoxemia of the respiratory center would tend to produce overventilation and alkalosis. In extreme degrees of shock when oxygen intake fails to keep pace with oxygen requirement, oxygen debt occurs, lactic acid accumulates and acidosis results. Koehler, Brunquist and Loevenhart³² have demonstrated that arterial anoxemia causes an initial alkalosis which is succeeded by acidosis if the anoxemia continues. There is no reason to assume that stagnant anoxemia has a different action from arterial anoxemia. In the long run both exert similar effects on the tissues.

Thus, acapnia and acidosis are both to be regarded as characteristic of shock. They come at different degrees. Both are at least partially dependent on diminished blood flow, and neither is the cause of shock.

One other point is noteworthy in regard to the anoxemia. Harrison and Blalock³³ demonstrated that severe anoxemia increases minute cardiac output, and Harrison, Wilson, Neighbors and Pilcher³⁴ have demonstrated that mild anoxemia often has a similar effect. In shock tissue anoxemia is present in marked degree. Despite this stimulus the minute cardiac output remains low because of the insufficient volume

30 Cannon, W. B. Acidosis in Cases of Shock, Hemorrhage and Gas Infection, *J. A. M. A.* **70** 531 (Feb. 23) 1918.

31 Wilson, D. W. Neutrality Regulations in the Body, *Physiol. Rev.* **3** 293 1923.

32 Koehler, A. E., Brunquist, E., and Loevenhart, A. The Cause of Death in Anoxemia, *J. Biol. Chem.* **64** 313, 1925.

33 Harrison, T. R., and Blalock, A. The Regulation of Circulation. VI. The Effects of Severe Anoxemia on the Cardiac Output of Dogs, *Am. J. Physiol.* **80** 169, 1927.

34 Harrison, T. R., Wilson, C. P., Neighbors, D., and Pilcher, C. To be published.

of the blood. As anoxemia is a more constant and stronger stimulant to the circulation in normal animals than any drug which has been studied, it is not to be expected than any drug can do—in striking degree—what the natural stimulus fails to do. From this point of view, the beneficial action of ephedrine is rather surprising. The diminished cardiac output, despite tissue anoxemia, constitutes another reason for saying that the primary object of treatment should be to restore the

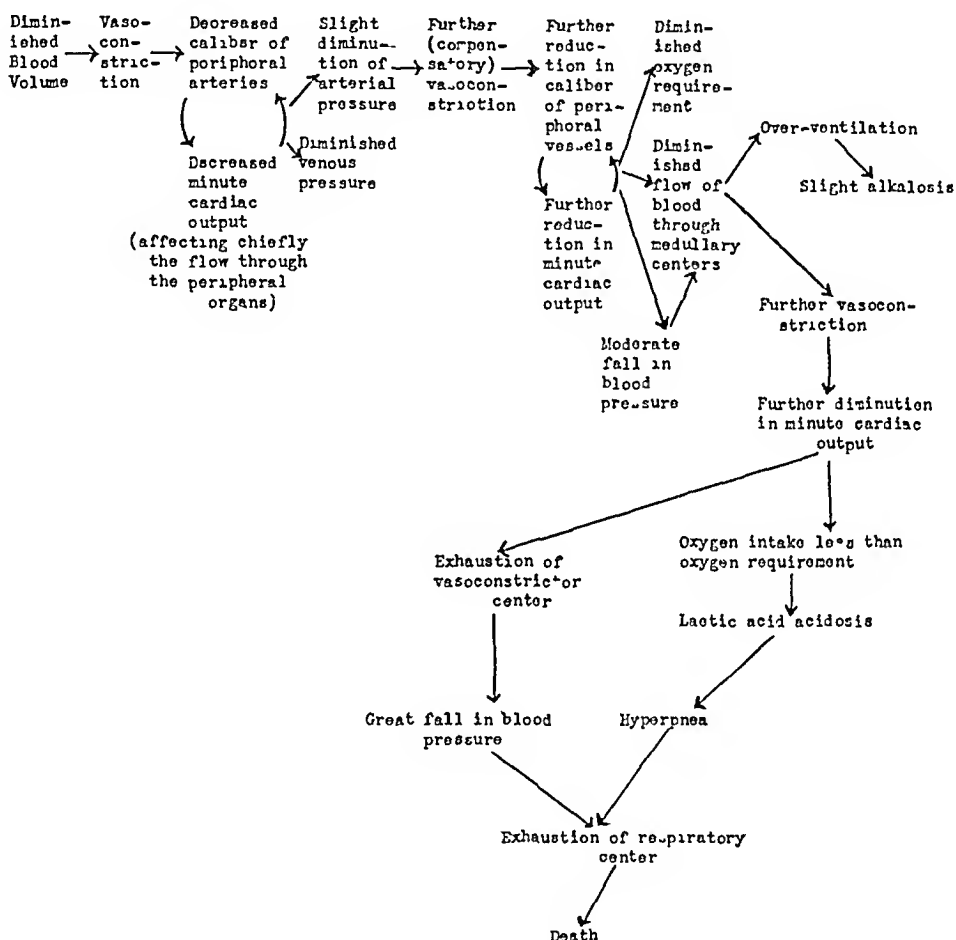


Chart 12—Successive steps in the mechanism of shock resulting from hemorrhage

volume of the blood. When this is done, the circulation responds to the stimulus of anoxemia, which is thereby diminished in degree.

The successive steps in the mechanism of shock resulting from hemorrhage would seem to be approximately as shown in chart 12.

Gesell's studies, as well as those of Wiggers, indicated an essential similarity between shock and hemorrhage so far as their effects on the circulation were concerned. My own observations on other types of shock than that following hemorrhage are far from completed, but they seem to indicate the same general relationship between mean blood pres-

sure and minute cardiac output as have been reported in this study. It appears, therefore, that the circulatory reactions in both hemorrhage and shock are results of a diminished circulating blood volume, initiated in the one case by loss of blood from the body and in the other by capillary dilatation—from histamine-like poisons, splanchnic vasodilatation or other causes—causing loss of circulating blood into the body. This conception is now generally accepted, and is in no sense original with me.

It is believed that the observations reported in this study are not without clinical significance, and some of the more important points in this connection will now be mentioned.

These experiments are more nearly comparable to clinical conditions than those previously reported, because the animals were not subjected to any operative procedure other than the insertion of an arterial cannula, and also because in several of the experiments no narcotic was used.

The results indicate quite definitely that no single factor of the blood pressure is of paramount value as a guide to incipient shock. The circulation has already become seriously impaired before significant changes in systolic blood pressure occur. The relationship existing between diastolic and systolic pressure or that existing between diastolic pressure and its previously known value are of significance. The pulse pressure and the pulse rate should be more satisfactory clinical guides, although, as has been pointed out, the pulse rate may remain normal after a notable decline in the minute cardiac output has occurred. The pulse rate always increases before the blood pressure diminishes and hence, of the two, is a better criterion of the onset of shock. Therapy should not be delayed until the blood pressure is definitely "below normal." A low level of blood pressure indicates a moribund patient, and even transfusion may be expected to fail often in such instances.

Any patient, who, after hemorrhage, has a significant tachycardia, should be treated for incipient shock.

In regard to the choice of therapeutic measures, the results of this study emphasize the relative uselessness of drugs as contrasted to the procedures which restore the volume of blood. These results are in accord with general clinical experience.

Digitalis is used frequently in treatment for shock. Because the drug is of great value in most types of circulatory failures due to cardiac disease, there seems to be a general impression that circulatory failure from any cause constitutes an indication for digitalis. The administration of digitalis preparations in shock cannot be too strongly condemned. Of all the therapeutic measures studied, digitalis was the most universally harmful. This conclusion is in accord with that drawn by Harrison and Leonard from their study of this drug in normal animals. I agree with their statements in reference to digitalis in shock.

The evidence presented suggests that when so used the drug may be harmful. As a matter of fact when digitalis is given to these patients it is often administered intramuscularly as digifolin in doses of one to three cubic centimeters a day, and such doses probably have no effect at all. If the drug were administered in full amount in such cases we should probably see harmful effects occasionally. As it is one does not usually observe any effect from digitalis in these patients.

Ether may be beneficial, but in some instances it is harmful. The same may be said of epinephrine hydrochloride. Both of these substances have too evanescent an action to be of any lasting value, and the immediate stimulation following their administration may be followed by depression. Epinephrine hydrochloride should never be given intravenously in shock, as the beneficial action lasts only a few minutes. The best results from ether were obtained by intra-arterial administration, a method which is impractical in the clinic, and dangerous, in any event.

Caffeine appears to do some good in mild shock. The optimum dose appears to be from 0.25 to 0.5 Gm. of the pure drug, or twice this amount of caffeine sodium benzoate for a patient of average size. Too much faith should not be placed in caffeine. It may be without value in moderate degrees of shock and is certainly without value in severe shock.

Ephedrine appears to be the best of the drugs. In animals moribund from extreme shock it appears sometimes to be harmful, but such instances are hopeless no matter what form of therapy is used. The effects of various doses of ephedrine have not been determined in this study. The beneficial effects in the animals followed doses of 2 mg. per kilogram (approximately 0.13 Gm., or 2 grains, for a patient weighing 140 pounds [63.5 Kg.]).

The value of saline infusion and transfusion in hemorrhage has been proved clinically. These experiments indicate that they should be employed early, before the blood pressure falls, and in abundant amounts.

The following procedures are suggested as a tentative routine treatment of any hemorrhage of significant magnitude. (Hemorrhage of more than 1 liter may probably be regarded as "significant" from this point of view.)

1. As soon as the patient is seen and the hemorrhage is controlled, he should be given from 65 to 130 mg. (1 to 2 grains) of ephedrine subcutaneously.

2. Intravenous saline infusion should be instituted as soon as possible, and relatively large amounts should be given. Ordinarily, one need not have any fear of "embarrassing the heart." Provided there is no structural cardiac disease and no pre-existing hypertension of severe degree, and the patient is under 60 years of age, the heart will be able to take care of any reasonable amount of fluid added to the circulation. During the first hour 1 liter of saline solution should be given into the

vein. Thereafter, subcutaneous infusion should be employed until transfusion can be carried out.

3 As soon as the saline infusion has been begun the preliminary measures (procuring a donor and matching the blood) for transfusion should be instituted. If the patient's condition appears relieved transfusion may not be necessary. If marked tachycardia persists, and more particularly if the systolic blood pressure is below 100 to 110, the transfusion should be performed.

4 If after the conclusion of transfusion, the patient's condition remains precarious, the whole process should be repeated.

It is admitted that by this routine plan of treatment a great many unnecessary transfusions will be done. It is believed however that severe shock will sometimes be prevented and a life which otherwise would be lost will occasionally be saved.

When the hemorrhage is from an internal organ and necessitates an operation, general anesthesia should not be used. The present work indicates that ether is dangerous. Previous work suggests that chloroform, which decreases minute cardiac output, and ethyl chloride which often has the same effect (Blalock²), would probably be distinctly harmful. Clinical experience and experimental results agree in indicating that local anesthesia should be employed for operations on patients who have bled profusely.

SUMMARY AND CONCLUSIONS

The pulse rate, consumption of oxygen, mean blood pressure and minute cardiac output have been studied before and after successive bleedings in morphinized dogs and in trained unnarcotized dogs. In a few experiments maximum and minimum arterial pressures were recorded. The methods which were used did not require any operative procedure except the insertion of an arterial cannula and cardiac punctures. Repeated hemorrhages cause a diminution in minute cardiac output, which usually precedes the increase in pulse rate and always precedes any significant fall in mean blood pressure. The minute cardiac output is usually from 30 to 50 per cent below the normal level before a marked diminution in mean blood pressure occurs.

These observations are interpreted as meaning that the essential circulatory effects of a diminished volume of blood are (1) decreased minute cardiac output and (2) diminished caliber of peripheral arteries. It is believed that the other circulatory effects are secondary. The blood pressure is an inadequate guide to the state of the circulation in incipient shock.

Various therapeutic measures have been instituted and their effects studied. In general it may be said that drugs are relatively useless as

compared to those measures which tend to restore blood volume. Transfusion of blood and intravenous saline infusion are beneficial, but they may fail in animals which have been in a severe state of shock for a considerable period. The effects of drugs may be summarized as follows: 1. Digitalis is always harmful. 2. Strychnine is usually useless. 3. Epinephrine hydrochloride and ether have uncertain actions, and their effects are too evanescent to be of lasting value in most instances. 4. Caffeine is slightly beneficial when the shock is not severe. 5. Ephedrine seems to be better than any of the drugs studied. It is more beneficial than caffeine, but much less so than the administration of fluid or blood.

On the basis of these observations certain physiologic considerations of shock are discussed, and a tentative routine treatment of severe hemorrhage is suggested.

A REVIEW OF UROLOGIC SURGERY

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KIDNEY

Surgical Technique—Chauvin¹ reported a case in which secondary nephrectomy was performed by means of thoracophrenolaparotomy. Several years previously the patient had been struck by a bullet which had broken the tenth rib, perforated the pleural culdesac and finally stopped in the right lobe of the liver. When the kidney was removed it was found embedded in a thick, hard, fibrous mass. As sufficient exposure could not be obtained even with resection of the twelfth rib the pleural culdesac and the diaphragm were incised up to the ninth rib which permitted ample operating space. Adhesions from an earlier empyema prevented pneumothorax.

Roseno² expressed the belief that pyelotomy is much superior to nephrotomy, if it can be performed. He stated that of 1767 nephrotomies reported in twenty-five years 85 were secondary, 102 patients died, a mortality of 5.8 per cent. In contrast to this, in 950 pyelotomies reported in seventeen years one of which was a secondary nephrectomy seven deaths occurred a mortality of 0.7 per cent. He attributed the more favorable results to the following reasons: (1) the opening is small and there is no cutting into the functioning parenchyma, (2) fistulas after pyelotomy are extremely rare, (3) the danger of operative and postoperative hemorrhage is slight and (4) even in adherent kidneys, approach to the pelvis is always possible, especially

1 Chauvin E. Néphrectomie secondaire par thoraco-phreno-laparotomie, *Press med* 35 250, 1927

2 Roseno, Alfred. Die Nephrotomie Ihre Bedeutung und der Weg zur Verhütung ihrer Gefahren, *Ztschr f Urol Chr* 20 96 1926

with Rosenstein's technic using the anterior wall of the pelvis. There are, however, several definite indications for nephrotomy.

1 Large stones that cannot be freed in any other manner, and stones that do not cast shadows or cannot be felt and are only demonstrated by splitting the kidney. Roseno reported such stones as occurring in from 1 to 4 per cent of cases in European clinics, while Braasch and Foulds found the following. In 146 cases, roentgenograms showed a single stone, but surgical exploration revealed more. In sixty-six cases roentgenogram showed multiple stones, and operation revealed but one. In twenty-one cases, roentgenogram did not show shadows, and operation showed one or more stones.

- 2 Early tuberculosis, exploratory nephrotomy
- 3 Small tumors of the kidney, exploratory nephrotomy
- 4 Congestion and bleeding from the capillaries of the papillae
- 5 Injuries to the kidney
- 6 Recurring renal colic on the basis of unilateral nephritis
- 7 Suppurating renal infections associated with firmly embedded stones or stag-horn calculi
- 8 Uremia due to nephritis or chronic obstruction

In 1880, Morris was the first to cut into the kidney and extract a stone. In 1888, Von Czerny performed the first pyelotomy. The operations were described as simple, harmless and successful. At first, Israel and LeDentu advised packing only, but they soon introduced suturing the parenchyma after nephrotomy. This was kept up until 1908, when Zuckerkandl popularized pyelotomy. Since then the indications for nephrotomy have decreased because of danger of hemorrhage, fistula and marked destruction of parenchyma.

The classic method (Tuffier) is briefly described. The kidney is entirely freed and a tourniquet put around the pedicle. Incision is made from pole to pole. After removal of the stone, the parenchyma is sutured together. These sutures must be tight to check all bleeding and eliminate all dead space between the cut surfaces. Because of the softness of the parenchyma, the sutures often cut in, this was somewhat overcome by using mattress sutures.

Various attempts were made to improve the technic of nephrotomy, such as the Zondek incision, the Marwedel right angle incision, the blunt method of Rovsing and Hochenegg, the sawing technic of Cullen, plastic covering of the wound with muscle tissue, with fat and with connective tissue, and the tying of sutures over fat pads, care in preventing opening the pelvis (Heymann), the drainage method through the parenchyma to the outside or through the ureter into the bladder and the combination of drainage with ureteral catheter and nephropexy (Rehn). All these, however, have failed to eliminate the dangers of nephrotomy. The usual complications have been operative and post-operative bleeding and the formation of fistula. Every incision destroys blood vessels and parenchyma, which leads to infarction.

followed by connective tissue organization and distortion of the normal adjacent parenchyma. The sutures also destroy the parenchyma by pressure atrophy. The problem has been to eliminate the use of sutures.

In the consideration of hemostasis, there are two types of bleeding in all wounds, parenchymal or oozing, and vascular. In the former there is danger if the patient is a "bleeder," or has a disease that may increase coagulation time, or if blood pressure is high as in arteriosclerosis. In both types it is difficult to secure thrombosis.

Often if blood vessels are cut they contract. Bleeding may not occur at the time, but later the vessels open and bleeding is profuse. This occasionally follows nephrotomy. Often the hemorrhage will continue until clots and coagulated blood are removed.

Three conditions are essential to prevent bleeding: (1) the formation of a clot should be prevented, (2) the nonactive blood vessels that may bleed later should be cared for, and (3) the cut surfaces should not be injured any more than is necessary.

Clinical observation shows three types of bleeding: (1) immediate at the time of operation, (2) shortly after operation and (3) from eight to fourteen days after operation. Bleeding in the wound leads to the splitting of sutures, and then bleeding into the perirenal tissues. Bleeding at operation from the large vessels is controlled immediately, this may be aided by Rovsing's incision or the multiple button-hole incisions of Magoun. The present treatment for postoperative hemorrhage is to pack and apply mattress sutures. Packing may cause bleeding when it is pulled out.

Roseno has suggested a change in technic. While there is no method of opening the kidney that will not tear blood vessels, he suggests that each vessel be carefully clamped and ligated. This puts the operation on an accurate and efficient hemostatic basis and leaves only slight oozing from the parenchyma which is of no consequence. He has applied this technic experimentally with good results. Both halves of the kidney will unite readily, there being no danger of later hemorrhage or the formation of a fistula, healing occurs with a minimum of scar formation. Anatomic studies have shown that there is no bridging of the scar by collateral circulation because all the vessels destroyed are terminal arteries.

From 1913 to 1925, 234 renal operations, of which 38 were nephrotomies, were performed in Roseno's clinic. Seven postoperative hemorrhages occurred, one stopped spontaneously, in two cases secondary operation was performed and the wound packed. The kidney was removed subsequently in one, in five secondary nephrectomy was performed, two patients died from the operation, and two patients died from urosepsis. The early work in this clinic was done by Israel

and Karewski, since Rosenstein has taken the service, all vessels in the wounds after nephrotomy have been ligated with better results

Williamson³ reported further work on transplantation of the kidney. He found that an autogenous transplant of the kidney will maintain the life of the experimental animal for several months after the removal of the other normal kidney. It was also found that during the time that the autogenous transplant is functioning, the urinary constituents are essentially normal and the animal behaves and lives normally. Because of contracture of the end of the ureter, however, hydronephrosis and infection supervene and cause the experiment to fail ultimately.

Homogenous and autogenous transplants function similarly, but only for a short period of several days except in rare instances. In these experiments in the animals with three functioning kidneys, two normal and one transplant, the blood urea was markedly reduced.

The site of the transplant does not materially lengthen the functional life or influence the terminal histologic picture, which is that of acute atypical glomerular nephritis followed by general acute nephritis. Infection as evidenced by the cytologic changes is not a factor in these experiments so long as good drainage and function are maintained. If the transplanted kidney is allowed to remain in place after aneuria develops there is a tendency for it to be replaced by fibrous tissue. The failure of homogenous transplants seems attributable to a biologic incompatibility between the donor and recipient. The value of the transplantation of the kidney as a clinical measure is questionable with our present knowledge, although under proper conditions it might be worthy of serious consideration.

Hinman and Morison,⁴ in experiments on rabbits, ligated and divided the left ureter and then killed the animals in from seven to seventy days. Two were killed at one time, in one an arterial injection was combined with the injection of both ureters.

These studies showed that the arterial circulation of the rabbit's kidney is distributed in two planes within the parenchyma in relation to the renal pelvis. The main subdivisions of the renal artery pass around circumferentially, while the finer branches are distributed radially to the cavity of the pelvis. With the production of hydronephrosis, the arterial circulation undergoes two phases of alteration. The first phase, occurring at the onset, is relatively short and appears usually to be due to purely mechanical interference. The second phase which soon follows, in addition to the mechanical interference, has a reduction

3 Williamson, C. S. Further Studies on the Transplantation of the Kidney, *J. Urol.* **16** 231, 1926.

4 Hinman, Frank and Morison, D. M. Experimental Hydronephrosis, Arterial Changes in the Progressive Hydronephrosis of Rabbits with Complete Ureteral Obstruction, *Surg. Gynec. Obst.* **42** 209, 1926.

in circulatory function causing atrophy and thereby accelerates the development of the hydronephrosis

When ureteral obstruction occurs, the renal pelvis dilates and causes progressive compression of the enveloping parenchyma. Since the finer arterial branches traverse the parenchyma in a direction radial to the cavity of the pelvis, they are subjected early to compression in their long axes and consequently become tortuous and foreshortened. On continued obstruction, the kidney increases in circumference and therefore all structures in the circumferential course are either stretched or lengthened. Since the arteries are elastic tubes, they become attenuated and the lumina become smaller, with the resultant reduction in blood supply leading to ischemia, loss of tissue-tone and progressive atrophy.

Callahan and Schultz⁵ reported a case of aneurysm of the renal artery and reviewed the literature. About half of the cases reported are traumatic in origin, the remainder are spontaneous. Arteriosclerosis, syphilis, embolism, or some antecedent infection is usually the cause of the spontaneous type. Traumatic aneurysm is nearly always false, and spontaneous aneurysm is usually true.

The most important sequelae are rupture into the pelvis, producing hematuria, rupture into the peritoneal cavity without consequent hematuria, and destruction of the kidney, the latter is characteristic of the false type, in comparison, true aneurysm causes little destruction of the renal substance.

Aneurysm of the renal artery causes abdominal pain which is closely followed by hematuria. The most valuable diagnostic sign is a palpable tumor in the region of the kidney. True aneurysm may persist for a long time without causing symptoms although hematuria, pain and tumor may occur. Practically all cases in which there are symptoms end fatally unless operation is performed, death occurring from two days to five years after onset. In the small true aneurysms the prognosis is much less serious, and in those which have become calcified rupture is improbable.

Of the twelve patients operated on, ten were cured and two died. Nephrectomy was performed in ten cases. Orth was able to turn out the clots and successfully suture the tear, and in the authors' case it was also possible to excise the sac and preserve the artery. Orth reported good function a year later and in the case reported by Callahan and Schultz function was still good six months following operation. In the authors' case a sacculated aneurysm was found in the renal artery, the sac was clamped then ligated and excised. The perforated artery was closed without sacrificing the artery or any part of the kidney.

⁵ Callahan W. P. and Schultz F. H. Aneurysm of the Renal Artery, Surg. Gynec. Obst. 43:724, 1926.

Dreyfuss,⁶ after analyzing and reviewing the literature on pelvic kidney, stated that pathologically there are two types, the occasional pseudopelvic or movable kidney should be distinguished from the true pelvic kidney. The pelvic kidney is recognized more by the various symptoms within the pelvis than by differential diagnosis. Even the freedom from symptoms for many years is not against the appearance of any complaints of pelvic kidney, for in the course of time changes occur that may aggravate the condition. The diagnosis is made by the pyelogram which also demonstrates the presence of the other normally placed kidney. The function of the latter should always be demonstrated before operation. The presence of a normal kidney indicates the removal of the pelvic kidney, since much suffering may be averted. Nephropexy will take care of acquired pelvic kidneys and those types that lie between movable kidney and dystopia.

[ED NOTE—From a surgical point of view, the treatment in cases of ectopic kidney does not differ essentially from the treatment given when the organ is in its normal position. The mere fact that the kidney did not rise to its normal position does not indicate that treatment is required. If the kidney is functioning normally in its malposition, under ordinary circumstances it should not be disturbed. Usually it is difficult to change the position of the ectopic kidney because the blood vessels in the pedicle are short and the kidney is rather firmly fixed.]

Lipshutz and Hoffman⁷ described a rather remarkable specimen showing in a composite form the important variations of the renal arteries and veins.

Variations in the renal arteries are perhaps more frequently met with than in other large arterial trunks, and the commonest variation is the presence of an additional renal artery. As many as five or six in one kidney have been reported. Abnormalities in form, position and development of the kidney in association with the accessory renal arteries may be noted. In general, the kidney deviates from its normal reniform shape in proportion to the number of vessels. In horseshoe kidneys additional renal vessels are the rule.

Organs that migrate far from their original position may retain vessels from this position or receive or incorporate vessels of the region invaded. The kidney, during its growth, migrates and undergoes rotation around its long axis. The instances of accessory renal arteries arising from the iliac arteries and from the middle sacral and inferior mesenteric arteries are to be considered as persisting embryonic vessels of the capillary plexus supplying the normal embryonic kidney.

6 Dreyfuss, Wilhelm. Beitrag zur Kenntnis der Beckenmiere, *Ztschr f Urol Chir* 19 277, 1926.

7 Lipshutz, Benjamin, and Hoffman, Clarence. Renal Arterial Variations and Extraperitoneal Abdominal Nephrectomy, *Ann Surg* 84 525, 1926.

An accessory superior or inferior polar renal artery may originate from the renal artery proper and not from the aorta, Eisendrath directs especial attention to this variation. Some type of renal arterial variation is present in from 20 to 33 per cent of all subjects.

Undoubtedly insufficient attention is paid to the variations in the renal veins which are subject to a greater range of variations than are the arteries, and surgically are just as important.

Attention is called to the frequent production of hydronephrosis from compression of the ureteropelvic juncture by an accessory inferior polar renal artery.

An extraperitoneal abdominal approach for nephrectomy is described. The parietal peritoneum is stripped back carefully with elevation of the colon forward from the renal fossa. In this way the renal pedicle may be ligated primarily before the kidney is displaced, accessory vessels are dealt with, the danger of tear into the inferior vena cava is obviated and congenital anomalies, such as horseshoe kidney and ectopia can be better managed. The extraperitoneal abdominal route, according to these observers, finds more than rational application in the removal of large cysts and tumors of the kidney.

[ED NOTE—The problem of stripping back the parietal peritoneum it would seem, usually has not been solved easily by surgeons. Many prefer the abdominal direct transperitoneal route for large tumors. Largely on theoretical grounds one would have to determine whether to use extraperitoneal or transperitoneal methods according to the size of the tumor, according to the ease with which the peritoneum strips away from the renal fossa and its adherence to tumor or inflammatory tissue.]

Renal Tumors—Bothe⁸ reviewed the conceptions of the genesis of hypernephroma which have been held by various pathologists and urologists from the time of Grawitz. The results of a survey of the voluminous literature show that the following theories have been propounded:

- 1 Hydronephromas originate in suprarenal cell-rests
- 2 They are alveolar sarcomas having nothing to do with cell-rests
- 3 They are endotheliomas that originate from the endothelial lining of perivascular lymph spaces
- 4 They are classified, if benign, as adenoma, if malignant, as carcinoma
- 5 They develop from the endothelial cells lining the blood vascular spaces
- 6 They are derived from the epithelium lining the uriniferous tubules
- 7 They originate from islands of embryonic nephrogenic tissue

Bothe then considered the embryology of the suprarenal glands and the kidney, showing how these organs develop in juxtaposition and are intimately related in the relative position of their various anlagen.

⁸ Bothe A E. Hypernephromata, Ann Surg 84 57 1926

From a study of pig and human embryos in early stages, he showed that suprarenal rests may be encountered frequently in renal tissue, which may give rise to hypernephromatous neoplasia

From chemical studies comparing the amount of ether-soluble material, cholesterol and lecithin in hypernephroma and suprarenal tissue, Bothe concluded that there is a striking similarity between the two. Likewise the injection of watery extracts of hypernephroma tissue into rabbits causes a rise in blood sugar and glycosuria, a feature suggestive of the relationship of hypernephromatous tissue to the cortex cells of the suprarenal gland

The pathologic study of a series of nineteen cases from necropsy records at the University of Pennsylvania is tabulated. Three instances of hypernephroma in animals are cited

Bothe showed that it is not uncommon for the neoplasm to grow into the lumen of the renal veins, as is well known, and also at times to invade the wall of the vein. Likewise the tumor may grow into the lumen of the ureter, but rarely invades the ureteral walls. While hypernephroma usually arises primarily in the kidney it is rarely found as a primary tumor in other organs such as the liver, falciform ligament, pelvis, uterus, suprarenal gland, tongue, ovary, broad ligament, spermatic cords, testis, retroperitoneal tissue, pancreas and ciliary body, instances of which are cited

Metastatic hypernephroma is a reproduction in structure of the original tumor. The bones, lungs and liver are common sites. Metastasis may be an early feature of the disease and the growth in the kidney may be undemonstrable when the secondary growths may be prominent

The tumor is prone to develop in the male. It usually occurs between the ages of 40 and 60 years

In discussing pathology, Bothe showed that benign suprarenal rests are frequently found in renal tissue. They resemble, in histologic detail, the cells of the suprarenal gland. In a large microscopic section, he showed suprarenal rest tissue lying close to the proliferating hypernephromatous tissue, and considered that this indicated the possibility of hypernephromatous change in a suprarenal rest

In general, Bothe concluded from his studies that from the embryologic, pathologic and chemical standpoints hypernephroma arises in a manner in accord with the views originally presented by Grawitz

[ED. NOTE.—Bothe's study is exhaustive and represents an excellent review of a moot subject. To just what degree he has demonstrated the correctness of his contention will be subject to dispute. While the evidence is not conclusive it does argue strongly for the suprarenal rest hypothesis which has suffered considerably during the last decade at the hands of various pathologists. It is difficult to anticipate just

what interpretation would be made of the author's large sections showing suprarenal rests and hypernephroma in the same section, by those who hold to the endothelial or renal-cell genesis. At any rate this article will not pass without considerable comment as it revives the grawitzian theory and will stimulate other studies leading to its support or refutation.]

Vercesi⁹ described a case of a large primordial sarcoma of the kidney in a fetus. Histologically, he found that round and spindle-shaped cell types predominated. Vercesi believed that these cells belong to the homogenous and lymphogenous endothelial variety. The tumor in this case was large enough to cause dystocia. The mother was found to have syphilis.

Marion¹⁰ said that pyelography is of some help in the diagnosis of renal tumors, but that it should not be relied on entirely or regarded with too much importance, and that it is of little diagnostic value in hemorrhagic diseases of the kidney unless the kidney is enlarged. Pyelography that does not reveal a tumor may lull the examiner to a false sense of security, and thus a tumor, if present, increases in size, on the other hand, a blood clot in the renal pelvis may suggest tumor. Hematuria with blood clots not suggestive of tuberculosis, calculus, hydronephrosis or pyelonephritis is sufficient indication for a surgical examination of the kidney without consideration of the pyelographic picture. If, however, the kidney is large and there is no hematuria, it is necessary to resort to a pyelogram in order to determine whether or not the enlargement is the result of neoplasm.

Nicolas¹¹ noted that Israel has described many cases of hematuria with renal tumors, but that more rarely these cases show methemoglobinuria, such a case is reported in that of a man, aged 30, with tumor of the left kidney.

Nicolas believed that some Grawitz tumors have a powerful hemolytic action. Similar cases have occasionally been observed associated with nephritis and renal stones. It has been shown that urine has definite antihemolytic action.

Hilman,¹² under the title of "substitutio renis adiposa," referred to those processes of fat deposition in association with urinary lithiasis and, more rarely, pyelitis or pyonephrosis. Primary atrophy of the

9 Vercesi, Carlo. Sarcoma del rene fetale. Contributio allo studio dei tumori nella vita endouterina della distocie fetali, *Folia gynaeec* 22 101, 1926.

10 Marion. La pyelographie dans le diagnostic des tumeurs du rein, *J d'urolog med et chir* 22 310, 1926.

11 Nicolas. Methämogloburie beim Grawitztumor, *Ztschr f urol Chir* 20 212, 1926.

12 Hilman A G. Ueber den Fettansatz der Nieren. Vestnik chirurgii i pogranichnch oblastej 4 213, 1925 abstr. *Ztschr f urol Chir* 20 367, 1926.

renal substance plays the important rôle in the pathologic process, the fatty tissue develops secondarily. Hilman believed that the atrophy and fat deposition occurred in calculous pyonephrosis as a result of slow development of the process and the destructive condition brought on by shrinkage. The disease is rare, the author having noted only sixteen cases in the literature. He reported a case of his own, that of a woman, aged 56, a huge, fatty kidney, which had developed on calculous pyonephrosis, was removed. Hilman concluded: 1 The process of fat deposition in the atrophying kidney originates from the renal capsule and fatty tissue of the renal pelvis. 2 The fat metaplasia of the renal connective tissue is of little importance. 3 The clinical diagnosis is difficult, as there are no definite clinical signs. 4 The term "lipomatose paranephritis" should not be used, the old French term *substitutio renis adiposa* being correct.

Suprarenal Tumors—Gibson¹³ stated that a differential diagnosis of tumors of the suprarenal glands from other growths, as well as between cortical and medullary tumors of the gland itself, as a rule, can be made by their clinical manifestations. The added information gained by urologic investigation is often of decided value.

Tumors of the suprarenals give rise to three distinct syndromes, the genitosuprarenal, the Hutchinson and the Pepper. The genitosuprarenal syndrome occurs only in cortical tumors (carcinoma, hyperplasia, adenoma) and is accompanied in the female by masculine characteristics, and in the male by precocious puberty. The adult male shows no characteristic sexual alterations. Cortical tumors occur as frequently in infancy and childhood as in the adult. Hypertension is frequently associated with cortical tumors. Pigmentation occurs rarely in cortical tumors and never in medullary tumors.

The common tumors of the suprarenal medulla are of the neurocytoma or sarcoma types, which are peculiar to infancy and childhood. They occur in two forms: the Pepper, characterized by rapid abdominal enlargement due to liver metastasis, and the Hutchinson, characterized by early metastasis to the orbit producing unilateral exophthalmos (already mentioned). The primary growth generally remains small and may only be discovered at necropsy. The prognosis is almost uniformly bad. The treatment is surgical and radiologic.

In a series of 47,069 cases in the University of California Hospital, nine were recorded as cases of suprarenal tumors. Of these only four were proved to be primary suprarenal tumors.

Renal Infections—Broglia¹⁴ stated that atrophic pyelonephritis constitutes the final stage of a process in which the ordinary trans-

13 Gibson, T. E. The Diagnosis of Adrenal Tumors, California & West Med 26 201, 1927.

14 Broglia, R. Pyelonephrite atrophique, J. d'urologie med. et chir. 22 8, 1926.

formation into pyonephrosis did not result, even though ureteral obstruction was present. The origin of the disease is obscure. He suggested as an hypothesis, that the atrophic pyelonephritis may be the final result of ascending chronic pyelonephritis in which the inflammatory process is marked in the renal parenchyma. There is preponderance of the factor "nephritis" over the factor "pyelitis," and extensive parenchymal destruction occurs before ureteral inflammation and obstruction. Pyelography is the most accurate means of investigation. It is not always possible on account of ureteral stricture and obstruction. The diagnosis is made on the evidence of pelvic dilatation without trace of small or large secondary cavities. Nephrectomy is the only procedure.

Atrophic pyelonephritis is distinguishable from chronic bilateral pyelonephritis from both clinical and pathologic points of view. The urinary symptoms are less severe and are usually not progressive, the pain is unilateral and may be more severe, and is often accompanied by evidences of acute renal infection. Usually only one kidney is affected, and, when removed, it is found to be greatly reduced in size. The atrophy may be confined largely to half of the kidney. On section marked cicatricial changes are apparent. There is often well-marked dilatation of the renal pelvis, although to a much less degree than that with primary hydronephrosis.

According to Braasch, atrophic pyelonephritis is not the end-result of the usual pyelonephritis. It can hardly be explained by primary stricture of the ureter with hydronephrosis and secondary atrophy since the dilatation of the pelvis is not sufficient to cause atrophy, and, furthermore, the atrophy is not symmetrical, but is frequently confined to one portion of the kidney. The possibility of a primary stricture of the ureter, with diffuse acute infection in the renal cortex and consequent atrophy, before the hydronephrotic sac is developed, may be considered.

Diseased kidneys are often small and difficult to find at operation. At times they are composed almost entirely of scar tissue and may not be more than 3 or 4 cm. in diameter. In spite of the apparently small amount of disease present removal of the atrophic kidney usually affords good results. In a series of cases in which operation was performed at the Mayo Clinic, improvement or cessation of vesical symptoms and improvement of the general condition have been accomplished for practically every patient.

Mercier and Perard¹⁵ observed a patient who exhibited marked hematuria from the left kidney about two years after nephrectomy had been performed on the right side for tuberculosis. The hematuria appeared suddenly without other symptoms. The bleeding was observed

¹⁵ Mercier, O., and Perard, J. Un cas d'hématurie abondante de pyelonephrite arrêtee par le catheterisme ureteral, *J d'urolog med et chir* 22 304, 1926

through the cystoscope. An injection of a few centimeters of silver nitrate stopped the hemorrhage immediately. Numerous colon bacilli were found in the urine. The authors stress the fact that from a diagnostic standpoint abundant hematuria from a healthy kidney after nephrectomy for tuberculosis does not always signify a new focus of tuberculosis. It may be caused by ordinary infection from colon bacilli.

Smunow¹⁶ called attention to the rarity of carbuncle of the kidney, only twenty-one true cases being recorded, including five of his own. These five showed staphylococcus infection, four *Staphylococcus aureus* and one, staphylococcus and diplococcus of Frankel. In three cases the portal of entry was the respiratory tract, while in two it was unknown. One patient gave a history of renal trauma and ptosis.

Until recently it has been believed that such cases are secondary to infections of skin or bone. There has been no previous mention in the literature of the respiratory tract as a portal of entry, hence the hypothesis that hematogenous infection of the kidney comes from the mucous membrane of the respiratory tract.

Three of Smunow's patients were males and two were females. Among other patients noted, fifteen were men and one was a woman.

The course is acute, but not stormy. There is constant fever, dull lumbar pain and muscle rigidity. Palpation reveals a large tender kidney. Pressure in the twelfth costovertebral angle causes pain. The urine contains pus and red blood cells. Cultures of the urine are usually sterile. Functionally, the appearance of the indigo carmine is delayed in the affected kidney. The procedure used is nephrectomy.

Renal Tuberculosis.—Forged¹⁷ noted that the triad, sterile pyuria, albumin and the bacilli of tuberculosis, may be missing either partially or completely in advanced renal tuberculosis. Three hundred and one cases were investigated with this in mind. Only those cases were accepted in which clinical or pathologic examination revealed that the pelvis and ureter were patent. Fourteen such cases were free from albumin, among these were six cases in which tuberculous processes, which macroscopically had no connection with the pelvis, were walled off. In one or two cases with definite connection between the cavernous process and the pelvis there was entire destruction of the renal parenchyma, while in the other there was a large abscess in the lower pole which delayed drainage. In two cases ureteral obstruction prevented drainage into the bladder, in one case the obstruction was a stone and in the other a ureteral kink. In four other cases the reason

16 Smunow, A. W. Ueber Nierenkarbunkel. *Ztschr. f. urol. Chm.* **20** 243 1926.

17 Forged, Jens. Nieren tuberkulose ohne charakteristischen Harnbefund, *Bibliot. f. Læger* **117** 269 1926 abstr., *Ztschr. f. urol. Chm.* **19** 416 1926.

for the missing albuminuria could not be established. In still two other cases there was neither continuous nor intermittent pyuria.

[ED NOTE—At times the paucity of urinary symptoms is marked even if advanced renal tuberculosis is present. In rare cases an area of bullous edema simulating papillary tumor may be seen partially occluding the ureteral orifice. In other cases there is mild generalized cystitis. There is practically always diminished renal function on the infected side.]

The most common type of renal tuberculosis occurring without symptoms of the bladder is the occluded type not included in Forged's series. Even in these cases of obstruction blood and pus are usually found. Braasch, in a series of sixty-seven cases of occlusion, found pus and red blood cells in all but eight. As a rule the urinary evidence of disease was not gross and urinalysis showed only a moderate number of cells.]

Ward¹⁸ reported a most interesting case of urinary calculi composed entirely of colon bacilli. The patient, a young woman, gave a history of attacks of diarrhea. For fifteen months she had suffered from renal colic intermittently. About three months later several small soft stones were passed. A pyelogram showed a somewhat ptosed right kidney with a kink in the ureter and a filling defect in the pelvis due to stones. Later nephrectomy was performed and many stones composed of colon bacilli were found.

Soft concretions are rare, and most of the soft stones reported are composed of fibrin-like material. Israel, in his recent book, mentions references to four cases similar to the one recorded.

Syphilis of the Kidney—Isaac-Krieger¹⁹ asserted that nephrositis is the most significant of syphilitic diseases of the kidney. It consists of degenerative changes of the epithelium in the collecting tubules. The acute form is characterized by generalized edema and transudation, albuminuria reaching as high as 50 per cent and lipoiduria, hypertension and changes in the eyegrounds are usually absent. There is no increased nitrogen retention in the blood. With immediate treatment, recovery is rapid. Without treatment the condition passes into the chronic form. Distinction from glomerulonephritis is made by the absence of increased blood pressure and hematuria. Dietetically there need be no decrease in the intake of albumin, but the amount of salt must be limited. Small doses of arsphenamine (0.15 Gm.) are given. Mercury is not used in the treatment, but bismuth may be given.

18 Ward R O. Urinary Calculi Composed of Bacteria. *Brit J Surg* **11** 230, 1926.

19 Isaac-Krieger, Karl. Die Lues der Nieren, *Ztschr f ärztl Fortbild* **23** 143 1926 abstr *Ztschr urol Chir* **20** 427, 1926.

The disease gradually develops into chronic nephrosis without edema, there may be slight edema of the ankles with continual ascites. The complications are bronchitis, sepsis and peritonitis. Further development may lead to amyloid degeneration or contracted kidney. In the latter condition it is not markedly different from true contracted kidney. At this stage hypertension, polyuria, nocturia, cardiac hypertrophy, edema, albuminuria and scanty urinary sediment may be seen. Antisyphilitic treatment must be handled carefully at this stage.

Renal Cysts—Löffler²⁰ stated that retention cysts of the kidney are either single or multiple and are often found by the pathologist. As they may not cause symptoms they are less often found by the clinician. The larger cysts sometimes fill the abdominal cavity and cause symptoms by pressure on adjacent organs. They may not, however, cause symptoms, the smaller cysts may give much trouble.

The cysts are usually in the lower pole, less often in the upper pole, and seldom on the convex border or sides of the kidney.

Löffler cited four cases. In the first case a large cyst in the lower pole of the left kidney caused increased mobility of the kidney and compressed the colon and stomach. In the second case there were two cysts on the convex border and another "the size of an apple" in the lower pole of the left kidney. In the third case the solitary cyst "the size of an orange" was at the lower pole of the right kidney pressing on the colon. In the first and third cases, the diagnosis was made by palpation, while in the second case the mass was thought to be a renal tumor. In the fourth case there was renal colic with deficient function from the left kidney. At operation the kidney was found to be normal, but a dark, livid "cherry-sized" tumor projected from the hilum, compressing the renal pelvis. It was thought to be malignant, and nephrectomy was performed. Pathologically, it was a small renal cyst which had grown out from the hilum. Similar cases are rare, the author found only two in the literature (Israel and Herriek). The usual procedure is nephrectomy. Löffler believed that if function is good, the cyst should be resected, as was done in two of his cases.

[ED. NOTE—Large renal cysts, which may occur at either pole of the kidney, usually the lower, may be resected readily and rarely cause marked impairment of renal function. Some of these cysts shell out of the kidney and leave flaps of renal substance that approximate readily to form a normal appearing kidney. Cysts of long standing usually have fairly thick walls and at times may be removed intact without rupture.]

²⁰ Löffler, Leopold. Zur Klinik der Nierencysten, *Ztschr. f. urol. Chir.* 20: 407, 1926.

Renal cysts cause pyelographic deformity similar to that of an extrarenal tumor, there may be obliteration of one of the calices, but the calix is rarely drawn out or attenuated as occurs with renal neoplasms. Usually few symptoms suggestive of a renal lesion are present.]

Tests of Function—Damski²¹ stated that pus in the renal region, originating primarily by way of the vascular system and secondarily from various diseases of the abdominal organs and the kidneys, belongs to that field of surgery which has not been satisfactorily explained. The etiology is still obscure and it is often extremely difficult to make an exact diagnosis. The relationship of perinephritic abscess to the various renal diseases which may necessitate nephrectomy is important. Many surgeons merely drain the abscess without further exploration.

After citing several cases, Damski concluded that (1) in cases of perinephritic abscess with normal urine, urologic investigation is indispensable, (2) the amount of urine from the diseased kidney does not always indicate the pathologic condition of that kidney, following the opening of such a perinephritic abscess, the kidney should be carefully explored, (3) in cases in which exploration is not feasible, following the disappearance of fever and other toxic signs, urologic examination should be carried out to determine the exact status of such a kidney, and (4) any abnormality of the urine from the diseased renal area must be given due consideration, in comparison with the urine from the normal side. Damski stated that there may be diminution of the output of indigo carmine from the kidney.

Blanc²² said that the phenolsulphonphthalein test is universally recognized as of considerable value in the study of renal function. The test must be carried out accurately if surgical procedure is to be decided, or if the function of each kidney is to be determined. Blanc favors the intravenous injection, since it is more accurate than the subcutaneous. Two conditions are essential for accurate results: all of the injection must pass into the vein and exactly 6 mg. of phenolsulphonphthalein should be injected. Blanc proposes the use of a graduated syringe and suggests diluting the 6 mg. of phenolsulphonphthalein to 4 cc. The results thus obtained are constant. A healthy kidney should eliminate from 30 to 35 per cent in seventy minutes, the total elimination should therefore be from 60 to 70 per cent.

Hinman and Veck²³ stated that under gradually increasing pressure in the renal pelvis there is a back flow of the pelvic contents into the

21 Damski, A. Einige Bemerkungen über den Wert des Ureterenkatheterismus und der Indigocarminprobe bei paranephritischen Eiterungen. *Ztschr. f. urol. Chir.* 20: 401, 1926.

22 Blanc, A. H. À propos de la technique de l'épreuve de la P. S. P. en chirurgie urinaire. *J. d'urolog. med. et chir.* 22: 17, 1926.

23 Hinman, Frank, and Veck, Morrell. Pyelovenous Back Flow. The Fate of Phenolsulphonphthalein in a Normal Renal Pelvis with the Ureter Tied. *J. Urol.* 15: 267, 1926.

renal vein, and the back pressure producing it is less than the excretory pressure. When this back flow has once been established, it will continue under low pressure. In experiments on rabbits, 2 cc of phenol-sulphonphthalein was injected slowly into the renal pelvis and the ureter ligated. Three of these animals were killed after twenty-four hours, three after forty-eight hours, two after ninety-six hours, and three after one hundred and sixty-eight hours. The bladder was catheterized in each case at the end of twenty-four and forty-eight hours and the amount of dye estimated. It was found that practically all the dye disappeared from the pelvis within four days and that little was left after two days. These observations indicate that an active flow of the dye occurred through the completely tied off renal pelvis. In conclusion Hinman and Veckl stated that the content of a closed hydronephrotic sac is neither cumulative nor stagnant but undergoes a continuous change fresh material being removed by active reabsorption which occurs mainly through pyelovenous back flow.

Fluoroscopy—Cross²⁴ advised the injection of opaque mediums for pyelograms under the guidance of vision. He believed that greater accuracy is maintained by injecting the kidney under observation with the fluoroscope, and since one may observe the flow down the ureter while the injection proceeds, there is less danger of overdistention of these delicate structures. The mobility of the kidney is easily ascertained, the change from the normal action is observed, and when stones that have not been suspected are encountered, turning the patient as the filling is in progress will give valuable information in the interpretation of the roentgenograms.

Legueu²⁵ stated that pyeloscopy, fluoroscopy of the renal pelvis, is of more value than pyelography in diagnosis. He has used this procedure in more than 700 cases and believes that the correct use of it requires considerable experience. The technic is well established the catheter is inserted into the pelvis and a syringe injection of sodium iodide carefully and slowly made, the progress of the injection is noted under the fluoroscopic screen. He said that there are two different types of pelvic contractions, "contractions en masse" and "contractions speciales," the pelvis and ureters acting similarly to the stomach. The evacuation of the pelvis lasts from two to ten minutes, the short contractions being produced at a rate of from five to six a minute. Legueu suggested that there may be a pyelo-ureteral sphincter which opens intermittently, the ureters having automatic contractions. From a

24 Cross, W. W. The Fluoroscope as an Aid to Making Pyelograms, *J Urol* 16 37, 1926

25 Legueu. La physiologie normale et pathologique etudiee a l'aide de la pyeloscopie, *Scalpel* 79 1027, 1927

pathologic standpoint, Legueu found that in certain types of hydronephrosis evacuation does not occur, the retention is complete, whereas in other cases the retention is incomplete and retarded. In some cases hyperkinetic movements with spasmodic contractions are observed. Hydronephrosis in such a case might be explained as being produced by a neuromuscular disturbance of dynamic origin and mechanical influence would play only an accessory rôle. The study of the pelvic musculature is also of importance in establishing the prognosis of pyelonephritis due to the colon bacillus, if the infected secretion is not kept in the pelvis through complete retention, the prognosis may be more satisfactory.

URETER

Tumors—Stewart²⁶ asserted that tumors of the ureter are usually of the papillary form. Any portion of the ureter may be affected, although there is evidently a predilection for either the upper or the lower portion. The symptoms produced are not pathognomonic and are the same as those engendered by renal neoplasm, namely, hematuria, pain, and sometimes renal enlargement because the tumor obstructs the ureter and causes hydronephrosis. Accurate diagnosis is usually difficult, but considerable aid is obtained from the employment of ureteral catheterization and pyelo-ureterography. It is important to determine the downward extent of the tumor, with special reference to the possibility of multiple growths. Radical operation is indicated. In most instances, nephro-ureterectomy, either complete or partial, is the method of choice.

Stones—Rathbun²⁷ pointed out that a large number of ureteral calculi pass spontaneously. Those which do not pass spontaneously and which show a tendency to lodge in one portion of the ureter possess greater potentiality for harm and require more careful consideration than those that are confined to the renal pelvis or one of the calices. It is often difficult to decide when conservative treatment should be used. The small stones will usually pass but the large ones usually require surgical intervention. Rathbun advised dilatation with ordinary silk elastic bougies and catheters. He disapproved of metallic mechanical dilators and preferred fulguration to enlarge the ureteral orifices to the use of cutting scissors because the latter type of incision often closes too quickly.

Rathbun considered it a real problem to answer the question: How long are we warranted in using these conservative measures? This depends on several factors, one of which is the position, shape and mobility of the calculus. He is more hopeful in such cases if the stone

²⁶ Stewart R. L. Primary Tumors of the Ureter, Brit J Surg **13** 667, 1926

²⁷ Rathbun N. P. The Management of Ureter Calculi, J Urol **16** 255, 1926

is noted just above the sacral promontory or just above the intramural portion, particularly if roentgenograms show variation in position at different times. He is less optimistic if the stone is noted about midway between the bladder and the brim of the pelvis, particularly if repeated roentgenograms that are carefully studied do not show any variation in position. He has found the calculus so firmly embedded in the mucosa of the ureter that it was difficult to extract it through an open incision, and is confident that no amount of dilatation would have influenced its position in the slightest degree.

Ectopic Openings—Herbst and Polkey²⁸ reported the case of a young girl who had suffered from incontinence since birth, because a ureter from an extra pelvis of the right kidney opened into the vagina. Heminephrectomy effected a cure. They noted that Kilbane reported ninety-eight cases from the literature besides two of his own.

The condition occurs with about equal frequency in the two sexes, although the male presents fewer symptoms. Incontinence, both diurnal and nocturnal, associated with the normal act of micturition is usually noted. The history of incontinence dates back to infancy, and in most cases is constant, except in a few in which the ureter passed under the sphincter in such a way that incontinence is controlled intermittently. Male patients do not experience this incontinence since the openings are above the external sphincter, usually above the level of the colliculus. In 75 per cent of the reported cases the ectopic opening belonged to a supernumerary ureter, and this ureter always drained the upper pelvis of a double kidney.

Herbst and Polkey believed that exploration and heminephrectomy offer a valuable method of procedure for this anomaly, because the majority of such ectopic ureteral orifices belong to supernumerary ureters that drain a part of a double or fused kidney. Many of the ureters are distended and infection of the part of the kidney which they drain makes implantation of this group an uncertain method. In cases in which the lower end of the ureter is accessible and a study of the upper portion of the urinary tract fails to show any marked dilatation and infection, some type of implantation may be indicated.

[ED. NOTE—Early in embryonic life the proximal end of the ureter opens into the lower end of the wolffian duct, but under normal conditions at about the sixth week the ureter and duct divide and open separately. If the ureter does not become detached from the duct and accompany it in its downward course, the ureteral openings may be found in any of the organs developing from the urogenital sinus.]

Hartman and Copenhagen analyzed thirty-seven cases in which the ureters opened extravasically; fourteen were supernumerary. The

²⁸ Herbst, R. H. and Polkey, H. J. Ectopic Ureteral Openings, *J. Urol.* 17:61, 1927.

openings were in the urethra in six, in the vagina in eight, in the vestibule of the vagina in twenty-one and in Gartner's duct in two]

Fronstein²⁹ stated that the stump of a ureter remaining after nephrectomy produces peristaltic waves. These have been observed as long as twelve years after the kidney was removed. These waves are able to express pus from the ureteral stump into the bladder.

Fronstein believed that aside from strictures and stones, the tone of the ureter is a factor. A ureterogram should be made in all cases, and if negative the usual operation of the kidney may be performed. If any of the foregoing factors are present, ureterectomy should be performed.

Empyema of the ureteral stump is rare. Kummell reported four in 286 nephrectomies and Israel four in 900 nephrectomies. Hyman reported three cases. Strictures or stones were usually present. Fronstein observed three cases in twenty years. The duration may be long, ranging from six to twenty-three years, he believes therefore, that the condition sometimes occurs and is not found.

The procedure accepted by most observers is complete extirpation. Fowler opens the sack and drains it by sewing the drain to the edges of the wound.

PROSTATE

Hypertrophy—Cohen, Dodds and Webb,³⁰ because of lack of uniform views on the value of tests of renal function in relation to prostatectomy, investigated a series of cases particularly in reference to analysis of the blood. It was found that the nonprotein nitrogen content and uric acid content of the blood formed the best guide to prognosis. The upper limit of safety for the complete operation of prostatectomy was found to be 50 mg. of nonprotein nitrogen and 3.5 mg. of uric acid for each hundred cubic centimeters. Experience has shown that if there is an increase over this, it is advisable to perform preliminary suprapubic cystotomy. Enucleation can be carried out within the limits of safety. The urea content of the blood is much more unreliable than the nonprotein nitrogen and uric acid contents. A high urea content must always be regarded as a serious sign, but a low urea content cannot always be regarded as an indication of normal renal function. Laboratory data should always be considered in combination with the clinical data.

Pasteau³¹ classified diseases of the prostate and the indications for treatment. Hypertrophy necessitates treatment when it causes retention.

29. Fronstein, R. Das Empyem des Harnleiterstumpfes. *Z. chr. f. urol. Chir.* 20: 183, 1926.

30. Cohen, I., Dodds, E. C. and Webb, C. H. S. Observations Bearing Upon the Operation of Prostatectomy. *Brit. J. Surg.* 13: 656, 1921.

31. Pasteau, O. Indications opératoires des prostatectomies. *J. med. franç.* 16: 3, 1927.

If the urine is clear and the retention is chronic, prostatectomy is indicated, especially if there is also vesical distention, and catheterization should not be employed. If the urine is infected, catheterization is necessary and should be carried out before operation. There are two types of prostatic stones, the urethroprostatic and the intraprostatic. Large intraprostatic stones are an indication for prostatectomy. Stones of the bladder are much more rare since prostatectomy, which relieves urinary retention, is now more frequently performed. Surgical intervention is indicated in malignant tumors of the prostate, unless there is diffuse carcinosis.

Pasteau reviewed the symptoms which usually lead to prostatectomy. In cases of chronic retention with infection but without distention, the need for operation is not immediate and preoperative treatment should be employed. Operation should be performed at once in cases of acute retention, and in some cases of severe prostatic bleeding, prostatectomy may be a life-saving procedure.

The perineal route should be used only occasionally, for example, in cases of serious urinary infection or in malignant conditions. The suprapubic route should be used. In most cases, the two stage operation gives a much better prognosis than the one stage. Pasteau advised an interval of a month after cystostomy before enucleation of the prostate.

Bumpus³² reported the results of the use of the punch operation in 114 of his cases at the Mayo Clinic. In seventy-two cases, the Caulk cautery punch was used. The functional results were better because of the large amounts of tissue removed. Two serious difficulties were encountered, however, delayed bleeding and continued febrile reaction. It is considered that these inconveniences more than outweigh the difficulties of immediate hemostasis encountered with the knife puncture of the Young and Braasch type. The poor results in early cases in which the knife punch is used should be much more than overcome by the modification of the Braasch punch, with which much larger portions of tissue may be removed. Punch operations are ideal in the median-bar types of obstruction. Bumpus does not advise the use of a punch in cases in which the lateral lobe of the prostate occurs.

Legueu³³ used the roentgen ray intensively in a series of cases of prostatic hypertrophy but radical operation usually had to be instituted to relieve difficult urination. Occasionally irradiation was followed by marked induration of the prostate and perineum which might be confused with carcinoma. In one case in which this occurred operation was deferred for six months during which time most of the induration was

32 Bumpus H C Results of Punch Prostatectomy, *J Urol* **16** 59, 1926

33 Legueu De la radiotherapie de l'adenome prostatique, *J d'urol* **21** 170, 1926

absorbed. Operation revealed an intensely inflamed prostate. Lequesne believed that roentgen-ray treatment brought on definite malignant changes in one case. As a result of his experiments he believed the roentgen ray to be useless, dangerous and entirely incapable of even modifying the course of the disease.

De Beaufond²⁴ divided cases of prostatic hypertrophy into two groups, the recognized and the unrecognized. Unrecognized hypertrophy causing residual urine is a treacherous form. In the recognized cases intervention is not always indicated, the patient may have secondary congestion or prostatitis and should be treated by massage. In cases in which intervention is necessary various conditions must first be corrected. If patients have uremia, drainage is usually required. Perineal operation should be performed on elderly weak patients. In aseptic cases in which there is retention catheterization should be carried out with aseptic precautions, if catheterization must be frequent, the bladder should be drained.

Marion²⁵ stated that an intersicoprostatic diaphragm may develop even after successful prostatectomy. Sometimes it is possible to insert only a curved filiform catheter. This diaphragm is the result of exaggerated development of the spur which is most often left between the bladder and the space from which the prostate has been removed. Marion observed such a diaphragm on reopening a bladder because of retention following prostatectomy. The bladder appeared to be composed of two cavities, a large upper one and a small lower one separated by a diaphragm which almost entirely closed the bladder. Such a diaphragm is the result of faulty technic in operating. When the periurethral adenoma projects far into the bladder it is necessary to tear the bladder around the adenoma; instead of the mucous membrane closing it, if this is not done a floating flap is left which may constitute only a spur at first, but which later develops into a diaphragm. The flap which separates the bladder and the prostatic cavity. In a loose flap or edge of mucosa remains after removal of the prostate it should be torn with the finger at its juncture with the wall of the bladder. A postoperative diaphragm of this type must be distinguished from aberrant prostatic adenoma or a stricture consequent to a tear of the urethra far below the adenoma. Marion devised a special instrument to insert through the urethra to cut these flaps or diaphragms. It consisted of a "beak" surrounded by two blades. He used it successfully in four cases. If it is impossible to open the bladder through the urethra the bladder should be opened and the diaphragm cut.

²⁴ De Beaufond. Les prostates, p. 107. *Ann. Chir. Urol.* 1927.

²⁵ Marion G. *Urology*, 1927, p. 107. *Ann. Chir. Urol.* 1927.

Cassuto,³⁶ in fulgurating a median prostatic lobe with a MacCarthy urethroscope, noted a sudden violent explosion inside the bladder. As the bladder did not seem to be ruptured, he waited, ready to operate if peritoneal or other symptoms became alarming. A cystoscopic examination performed on the eighth day disclosed a slightly edematous bladder with large stellate cuts on all its surface. Cassuto believed that the gas accumulating from the carbonization of the tissues exploded. Saint Cene, who reported two analogous cases, found that the explosion took place on fulgurating near the upper surfaces of the bladder where gas accumulates.

Michon³⁷ stated that occasionally cases are noted in which all the signs and symptoms of prostatic obstruction are exhibited and in which, nevertheless, it is clinically impossible to find the suspected enlargement. Symptoms such as dysuria, stagnation of urine, complete or incomplete retention and distention are not found alone in association with large prostates; there is no definite or constant relationship between the size of the prostate and the extent of the symptoms present. However, retention in the acute form is exceptional in cases in which there are prostatic symptoms but no enlarged prostate; in contrast to this, chronic, insidious retention, revealing itself only when there is distention, is not infrequently an accompaniment of the so-called prostate sans prostate. It is impossible in some cases with the most accurate examination and with the help of endoscopy, to discover the lesion. Histologic examinations alone, in spite of the absence of any objective signs, will permit the inclusion of this type of case in the group of prostatic cases and will suggest the kind of procedure that is used when the prostate is definitely hypertrophied, namely prostatectomy.

In the type of case presenting all the signs and symptoms of prostatism, even though the prostate is not large, prostatectomy should be performed. Even though it may not be apparent, there is usually a local lesion present and prostatectomy will relieve all the symptoms.

Thomas³⁸ outlined the preoperative care in prostatic cases as comprising drainage of the bladder and renal decompression, physical treatment and drugs when necessary, determination of the operability of the patient and determination of the best method of surgical intervention.

In practically all cases of prostatic obstruction with either complete or partial retention of urine, the factor of primary and paramount importance is drainage of the bladder in order to relieve urinary back-pressure on the kidneys. This procedure may be satisfactorily carried out either by intermittent or continuous catheterization or by cystotomy.

36 Cassuto, Augusto. Explosion dans la vessie au cours d'une electro-coagulation, *J. d'urolog. med. et chir.* **22** 263, 1926.

37 Michon, Louis. Prostaties sans prostates, *J. med. franç.* **16** 14, 1927.

38 Thomas, B. A. Preoperative Care of Patients with Prostatic Obstructions, *J. Urol.* **17** 87, 1927.

The much discussed question of drainage by catheter versus cystotomy or so-called one-stage versus two-stage prostatectomy seems still to be far from solution. Thomas reserves cystostomy for only a few patients, about 13 per cent.

Avoidance of constipation, forcing fluids and relief of back-pressure are the chief measures employed. Thorough physical examination should be made in all cases. The routine practice of Thomas in a study of renal function is the determination of the index of elimination of phenolsulphonphthalein or indigo carmine a day or two after admission and also on the same day the determinations of the blood urea nitrogen, blood sugar and coagulation time of the blood are made. Determination of the coagulation time will occasionally help one detect a bleeder. Treatment directed to hyperglycemia when it exists will facilitate convalescence. If the patient is found to have nitrogen retention the blood urea test is repeated weekly. Values up to 20 mg. for each hundred cubic centimeters of blood are regarded as excellent prognostically, from 20 to 30 mg. as borderline but not prohibiting operation if everything else is satisfactory, and over 30 mg., as contraindicative of prostatectomy at that time. The index of elimination of any of the dyes, phenol-sulphonphthalein having the preference for colorimetry in most laboratories, is probably sufficient. It gives a better idea of the stability of the renal function, which is the factor with which we are most concerned and is easier of application than any of the biochemical blood tests.

Low blood pressure is as bad as high blood pressure. A patient with systolic pressure of less than 110 must have a diastolic of more than 60, and a patient with diastolic pressure of less than 60 must have a systolic of more than 110. In such cases digitalization may turn the tide in favor of stage operative intervention.

[*ED. NOTE*—One-stage prostatectomy is the operation usually preferred. It permits visualization, accurate hemostasis and thorough removal of the gland. Consequently, in large clinics in which the operations are performed by highly skilled surgeons preliminary drainage is carried out by means of a urethral catheter. On the other hand, many urologists consider the two-stage operation with preliminary cystostomy and later removal of the gland the safest procedure. In careful hands, with an accurately controlled preliminary period of observation, excellent results are obtained by either method. In the present period of accurate urologic diagnosis together with the series of excellent renal functional procedures, death from uremia following prostatectomy is rare.]

Kimney² believed that postoperative care in prostate cases should start with careful preoperative study and the proper choice of anesthetic.

²⁹ Kimney, W. H. Post-Operative Care of Prostatectomized Patients, *Urology*, Vol. 17, No. 1, 1927.

Careful operative technic with as little mutilation as possible of the surrounding structures and with attention to hemostasis, by thorough packing thereby preventing secondary hemorrhage, is of utmost importance. Fluid should be forced by hypodermoclysis or other methods. The cardiovascular system should be watched carefully. Cleanliness of the operative wound during convalescence and prophylaxis against infection of the genito-urinary tract are necessary. Elimination by all the natural means must be watched and encouraged.

Infection—Henry⁴⁰ asserted that suppurative prostatitis should be treated surgically as early as possible. This avoids serious complications which might develop into a comparatively benign condition. Small abscesses situated on the anterior portion of the gland near the urethra may be treated medically. Massage should not be carried out, vaccines are useless. The abscess may be evacuated surgically in several ways. In the urethral route a finger introduced into the rectum pushes the prostate forward, while a rigid sound, placed in the urethra, is directed with force through the posterior wall of the prostatic urethra. This method is dangerous, but it may be used successfully in cases in which the infection is entirely intraprostatic. In the rectal route an incision is made through the rectal mucosa, this method may be used in abscesses that protrude on the side of the rectum and do not open into the urethra.

The perineal route in operating is the most satisfactory, a urethral catheter is inserted to be used as a guide. Either a transverse or a vertical perineal incision may be used. The rectum is stripped from the posterior surface of the prostate and the abscess opened. All pockets are drained and packed with gauze. This method assures a successful outcome, usually without complications. If the abscess is opened into the urethra and fistula results, insertion of a permanent urethral catheter permits the fistula to heal.

Lavenant⁴¹ stated that conservative or medical treatment does not suffice for all types of prostatitis. Patients who have prostatitis of the sclerous type with a vesical bar causing retention should be treated by the Bottini method or by fulguration, those who have prostatitis with the formation of stones should be treated surgically. Certain surgeons have been able to remove prostatic stones through the urethra, but this leaves the prostate as a focus of infection, it should be removed entirely. Following suprapubic prostatectomy in some cases the remaining prostatic tissue may be treated by ordinary conservative methods, but occasionally a secondary perineal prostatectomy is necessary for complete cure.

40 Henry, Robert. Les grandes infections de la prostate. Absces de la prostate et phlegmons periprostatiques, *J med franç* **16** 26, 1927.

41 Lavenant, A. Les prostatites aiguës et chroniques et leur traitement, *J med franç* **16** 19, 1927.

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the bladder and relaxation of the sphincter muscles of the neck of the bladder and urethra. Difficulty in the expulsion of urine, besides being caused by mechanical obstruction, may be due to diminished muscular power of the bladder, to increase in the tone of the sphincter muscles or to a combination of these two factors, resulting from a disturbance in nonsympathetic nervous control, while true vesical incontinence in the conscious person is probably rare except when there is interference with all three mechanisms. The control of the bladder, however, may be exercised by the spinal cord when part of the cord has been entirely separated from the higher centers, although such activity of the bladder is purely reflex and not under voluntary control.

Elsberg discussed disturbances of the bladder in cases of tumor of the brain, which occur in only one fourth of the cases, if those due to clouding of consciousness or psychic defect are excluded. In 165 patients with verified tumor of the brain, 60 had some disturbance of normal micturition, and 39 (23 per cent) had occasional or continued incontinence. Sixty-nine of the 165 patients were more or less disturbed mentally. In tumors of the frontal lobes mental disturbances were, of course, common, and in most of these cases some variety of vesical disturbances was present, incontinence being frequent. On the other hand, incontinence was infrequent when the growth was in some other portion of the brain. Excluding patients in stupor, coma, or with marked mental changes, urinary disturbances were no more frequent with subcortical than with cortical growths.

In tumors of the spinal cord disturbances of the bladder are noted much more frequently in the extramedullary, extradural, and conus and cauda types. In 80 per cent of the extramedullary, 84 per cent of the extradural and 60 per cent of the intramedullary growths such disturbances were present, but a tumor outside of the substance of the cord is more likely to cause disturbance than one within the substance. There is no particular segment of the cord especially concerned with control of the vesical sphincter. The lower the compression of the tumor is on the cord, however, the more common are the disturbances of the bladder.

Disturbances of the bladder usually appear late with tumors of the spinal cord, except in cases of extradural primary or secondary malignant disease in which the advance is rapid. Even if the tumor is in the sacral segments of the cord, where the nerve centers of the bladder lie, it is surprising that symptoms do not occur for at least a year. If tumors are within the substance of the cord, vesical disturbances, while much less common, appear earlier than with extramedullary growths.

The type of disturbance noted varied with the consistency of the tumor, the amount of compression of the cord and the rate of growth. Other things being equal, if the symptoms of the spinal cord have

lasted less than six months, difficulty in emptying the bladder is the most frequent, if they have lasted from six to twelve months, difficulty in urination or incontinence is frequent, and when the symptoms and signs of spinal compression have lasted several years or more, incontinence due either to overflow or to true paralysis of the sphincter muscle is most frequent

After removal of the tumor improvement in vesical control may occur rapidly. During the period that the patient is recovering vesical control, the contraction of the bladder is imperfect, and in consequence a number of ounces of residual urine are retained. Elsberg noted that the feeling of fullness in the bladder returns quickly if patients improve, as a rule before the return of somatic sensation. If prolonged pressure of the tumor has made recovery impossible, a pure spinal automatic control may appear in a few months.

Attention is called to the fact that we should not overlook purely genito-urinary disorders that may be associated with disease of the central nervous system and cause symptoms entirely independent of those due to lesion of the nerve.

[ED. NOTE—This article clears up a number of features concerning which urologists are frequently confused. While the act of micturition is not altogether explainable so far as detailed nervous mechanism is concerned, the ideas presented by Elsberg serve as a good basis for the practical explanation of the various features of the so-called cold bladder. Urologists often think only of the relaxed sphincter, vesical anesthesia, weak stream and fine trabeculation, which give the picture of the parietic bladder, without considering carefully the type of nerve lesion. As Elsberg notes, there is great opportunity for collaboration between the cystoscopist and the neurologist in correlating the disturbance of vesical mechanism with various types and sites of tumors during their growth and after their removal.]

Neoplasms—HARRIS,⁴⁴ in a 6 months female fetus, found a "pear shaped, apple sized" tumor which had pushed itself into the vesical neck. Histologically, it was composed of myxomatous connective tissue and was covered with plain epithelial cells. The musculature of the bladder was somewhat hypertrophied.

Perforation—Boss⁴⁵ recalled that the occurrence of spontaneous rupture of appendiceal abscess was well known to the surgeons of the nineteenth century, it was regarded as a good sign. Today rupture into the gastro-intestinal tract, bladder and other hollow organs is forestalled by early diagnosis and drainage.

⁴⁴ Harris, H. A. A Mesodermal Tumour of the Trigone of the Bladder in a Female Foetus of the Sixth Month, *J. Anat.* **60** 329, 1926.

⁴⁵ Boss, William. Perforation von appendicitischen Eiterungen in die Blase, *Ztschr. f. urol. Chir.* **20** 215, 1926.

Boss reported two cases of appendical rupture into the urinary bladder. The process usually is a slow one, which frequently adjusts itself. The pelvic fascias do not long resist an abscess and permit it to bore through. The contact of the pus with the vesical wall tends to cause retention and pain when the bladder empties. The vesical wall becomes thinner, helped by the opposing pressure of the urine, and finally rupture occurs. The differences of pressure causes disturbances in the circulation of the vesical wall and therefore enhances the tendency toward rupture. There may be no indication of the condition or there may be severe characteristic symptoms. There may be marked frequency and urgency with chills and fever for the first few days, leading occasionally to retention.

Cystoscopy does not show generalized cystitis, a circumscribed inflammatory reaction and bullous edema in the region of the perforation may be seen only occasionally. On the contrary, fistulas from adnexal perforations can be seen clearly. The urine contains fecoliths, fecal material, plant cells and muscle fibers, and has a fecal odor. Charcoal may be given by mouth and found in the urine, thereby demonstrating the fistulous connection.

The perforations usually heal spontaneously. They have been known to persist for as long as ten years. The bladder does not need particular attention.

Cecil⁴⁶ reported a case of sarcoma of the bladder in a man, aged 27. After suprapubic cystostomy and bilateral transplantation of the ureters to the rectum, total cystectomy was performed. The patient remained well for a year and nine months when a growth recurred in the abdominal wall and was excised by cautery shortly before the case was reported. Cecil also reviewed the literature, giving details of 193 cases of sarcoma of the bladder. From these cases he concluded that the gross appearance is not characteristic enough to distinguish it from other tumors. The tumor is usually situated on the base, trigone or vesical orifice, although it is found on the lateral and anterior walls more frequently than are epithelial tumors. Microscopically, it assumes all the varieties of sarcoma and has a marked tendency to invade the surrounding structures. It grows rapidly, and not infrequently multiple tumors are noted. Patients usually are young or past middle age, but they may be all ages. The tumors do not tend to metastasize and metastasis occurs late if at all. Hematuria is not constant. It is not even always present, and if present, is usually a late manifestation. Other symptoms also appear late. The diagnosis depends entirely on microscopic examination of the specimen. Resection is the method of choice in early cases. Irradiation has not been given sufficient trial, but it will probably prove inadequate. In most cases total cystectomy offers the only chance of cure.

⁴⁶ Cecil, H. L. Sarcoma of the Bladder, *J. Urol.* **16** 471, 1926.

Schmitz and Laibe⁴⁷ reported a series of fifty-two cases of inoperable advanced primary carcinoma of the urinary bladder in which the treatment consisted of radium, cautery and radium or roentgen rays, and roentgen rays alone. Satisfactory results were obtained with the massive, short-wave roentgen ray. The authors explained these good results by the carrying distribution of the intensity of radium and the roentgen ray and by the sensitiveness of the carcinoma to irradiation. They concluded that the short-wave roentgen ray applied according to modern methods is efficient in arresting the cancerous growth and in restoring the function of the bladder to normal.

Heilmann⁴⁸ described a pathologic anatomic lesion in the bladder of a woman, aged 73. There were numerous small white nodules the size of a pin, with a hemorrhagic halo, the center of which was sunken. There was also generalized cystitis. The urine was weakly acid and contained pus cells and colon bacilli. Microscopically, some of the nodules appeared as lymph follicles, sometimes with a large budding nucleus. Most of the follicles showed pathologic change, the capillaries were dilated and in the middle of the node were large, pale epithelioid cells undergoing degeneration, among which could be found granular masses. Some cells contained inclusions. A dense ring of lymphocytes could be seen about the nucleus. The larger plaques consisted chiefly of large polar cells. The flat epithelium of the wall of the bladder was missing over some of these plaques and some were necrotic. The entire picture suggested nodular cystitis and malakoplakia. The author believed that the malakoplakia developed from nodular cystitis.

Briggs and Maxwell⁴⁹ reported three cases of urinary leukoplakia. They also reported fifteen cases (five renal and ten vesical) that had been abstracted in the literature. If the urinary tract as a whole is considered, the condition is more common in men, however, the kidneys of men and women are affected equally. The renal pelvis is probably affected oftener than the bladder, in spite of the fact that vesical leukoplakia can be diagnosed by cystoscopy alone whereas the renal condition usually requires nephrectomy or necropsy for diagnosis. The condition may occur at any age. The average age at the time of diagnosis in the eighty cases was 41 years. It occurred earlier in the renal cases. Leukoplakia is probably present years before it is recognized, in each of the three cases reported by Briggs and Maxwell, urinary symptoms had been present for thirteen years.

47 Schmitz, Henry, and Laibe, J. E. F. Roentgen-Ray Treatment of Inoperable Carcinomas of the Urinary Bladder, *J. A. M. A.* **87** 1541 (Nov. 6) 1926.

48 Heilmann, P. Ueber Cystitis nodularis und Malakoplakie, *Beitr. z. path. Anat. u. z. allg. Path.* **75** 216, 1926.

49 Briggs, W. T., and Maxwell, E. S. Leucoplakia of the Urinary Tract, *J. Urol.* **16** 1, 1926.

Bacteriologic data at the present time is not sufficient to justify conclusions other than that infection of some type is usually associated with the lesion, in four cases, however, cultures of the urine were reported negative. The origin is unknown. Irritation in the form of infection or stone, or both, is often present but several cases have been reported in which bacteria were not discovered, and many in which there were no stones. While calculi may cause leukoplakia by irritation, one must not lose sight of the fact that desquamated cornified epithelium may act as a nucleus for stone, especially if infection is present. The symptoms are not pathognomonic. The passage of pieces of membrane, however, should always suggest leukoplakia. Leukoplakia of the bladder does not respond to irrigations or instillations, so resection, electrodesiccation or radium must be relied on, and none of these has been used often enough to judge its value. Since renal leukoplakia is seldom diagnosed before operation or necropsy, nephrectomy will usually be carried out for the associated pathologic lesion and not for leukoplakia.

Nedelec and Vafiadis⁵⁰ noted that vesical purpura may become apparent in infancy. Two thirds of the reported cases occurred in the female. The condition usually starts suddenly with fever, abdominal pain, pain in the extremities, dysuria and hematuria. The urine contains red blood cells, epithelial cells and rare hyaline casts. The capacity of the bladder remains normal and cystoscopy reveals round or irregular hemorrhagic areas of various sizes under the mucous membrane, these are situated especially round the trigone, floor of the bladder and the interureteric ridge. There are no signs of cystitis. The diagnosis is simple, especially in the presence of skin changes. Differential diagnosis must be made of tuberculosis, cystitis cystica and hemorrhagic cystitis. The prognosis of purpura is favorable and usually only symptomatic treatment is indicated. A case is described, that of a girl, aged 14, in which two blood transfusions effected cure. Twelve similar cases are cited from the literature.

Exstrophy—Robinson and Foulds⁵¹ reported the case of a man, aged 23, who was one of the five operated on for exstrophy of the bladder by Peters by his method of transplanting the ureters. This patient came under their care with pyonephrotic sac on the right side, which they drained. The patient recovered and is able to carry on in his trade twenty-one years after the transplantation of the ureters into the rectum.

(To be continued)

⁵⁰ Nedelec and Vafidis. Étude sur le purpura de la vessie, Arch d mal d org gén-urin **2** 257, 1925.

⁵¹ Robinson, T. A., and Foulds, G. S. The Late Results After an Operation for Exstrophy of the Bladder, Brit J Surg **14** 529, 1927.

PITUITARY ADAMANTINOMAS

REPORT OF THREE CASES *

MAX MINOR PEET, M D

ANN ARBOR, MICH

Pituitary adamantinomas are solid or cystic, benign or local malignant tumors. They contain enamel or enamel-forming tissue and develop from epithelial rests of the embryonic hypophyseal duct. Several types of tumors or tumor cysts have been described in the sella and the suprasellar regions, and much confusion has arisen regarding their classification and etiology. Some uniformity of nomenclature is slowly appearing, however, and today the classifications of certain types of tumors and their origins are generally accepted. Thus the most common tumor of the hypophysis is now regarded as an adenoma, while the cysts are believed to develop from embryologic remnants of the hypophyseal duct proper or from its extreme upper portion, the pouch of Rathke. Cysts or tumors arising from the duct are distinguished from those originating in Rathke's pouch by the squamous epithelium of the former contrasted with the cylindric, frequently ciliated, epithelial lining of the latter. Some authors still use the terms, "Rathke's pouch tumor" and "hypophyseal duct tumor" or "craniopharyngeal duct tumor" as synonymous, but there is a definite histologic distinction, and its general recognition will help materially to overcome the still prevalent confusion.

The exact embryologic anlage of the various cysts or tumors of the hypophyseal region is not only of academic interest, but of distinct clinical value. The cysts arising from Rathke's pouch develop between the anterior and posterior lobes of the pituitary and are, therefore, primarily intrasellar in origin. On the other hand, tumors of the hypophyseal duct, because of the rotation of the pituitary during its development, may occur at any point from the tuber cinereum at the base of the third ventricle, downward along the infundibulum to the anterior hypophyseal lobe. Erdheim¹ has shown that epithelial cell

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1 Erdheim, J. Zur normalen und pathologischen Histologie der Glandula thyreoidea, parathyreoidea und Hypophysis, *Beitr z path Anat u z allg Pathol* **33** 158, 1903, Ueber Hypophysenganggeschwulste und Hirncholesteatome, *Sitzungsber d k Akad d Wissensch Math-Naturw Cl, Wien* **113** 537, 1904, Ueber einen neuen Fall von Hypophysenganggeschwulst, *Centralbl f allg Pathol u path Anat* **17** 209 (March 31) 1906.

rests, remnants of the hypophyseal duct, can be demonstrated in 80 per cent of normal adults. These occur chiefly at two sites, an upper group is situated on the anterior aspect of the infundibulum near the third ventricle, and a lower group at the angle between the infundibulum and the anterior lobe. The majority of tumors of the hypophyseal duct found at operation or necropsy have originated in one or the other of these two locations.

Compared to the pituitary adenomas, the squamous epithelial tumors originating in the hypophyseal duct are relatively rare, only about sixty cases being recorded. These may be divided histologically, according to Duffy,² into three groups, first, the benign papillary cyst or intracystic papilloma, second, the benign or locally malignant adamantinoma which may be calcified or uncalcified, cystic or solid, the more complicated adamantinomas, the "authochthonous teratomas" of Ewing and the rarer tumors which resemble the cutaneous epithelioma, third, the rare spindle cell carcinoma with a tendency to metastasize.

The adamantinomas are the most common, comprising possibly half of the tumors originating in the hypophyseal duct. The resemblance between these tumors and those of the jaw was first noted by Onanoff³ in 1892. Luschka,⁴ in 1860, had found nests of squamous epithelium adjacent to the pituitary, but it remained for Erdheim in 1904 to suggest that these groups of epithelial cells were remnants of the embryonic hypophyseal-pharyngeal duct, and that the pituitary adamantinomas were in reality tumors of this origin. He coined the term "Hypophysenganggeschwulste" (tumor of the hypophyseal duct), which is now in general use.

The clinical picture varies with the exact location of the tumor, although nearly all show symptoms of hypopituitarism. The majority show obesity, many presenting the classic picture of the Frohlich syndrome, designated by Bartels⁵ as "dystrophia adiposogenitalis." Infantilism without adiposity (type Lorain) is occasionally observed. Neither gigantism nor acromegaly has been associated with an adamantinoma.

The general symptoms also vary with the age of onset. The two types just noted appear before puberty. In older patients who have

2 Duffy, William C. Hypophyseal Duct Tumors. A Report of Three Cases and a Fourth Case of Cyst of Rathke's Pouch, *Ann Surg* **72** 537 (Nov.) 1920.

3 Onanoff Jacques. Sur un cas d'epithelioma (etude histologique), Paris, 1892.

4 Luschka, Hubert. Der Hirnanhang und die Steissdruse des Menschen, Berlin, 1860.

5 Bartels, M. Ueber Plattenepithelgeschwulste der Hypophysengegend (des infundibulums), *Ztschr f Augenh* **16** 407 and 530, 1906, Ueber die Beziehungen von Veränderungen der Hypophysengegend zu Misswachstum und Genitalstörungen (Dystrophia adiposo-genitalis), *Munchen med Wchnschr* **55** 201 (Jan 28) 1908.

developed normally, the growth of the tumor tends to reverse the secondary sexual characteristics. In a man the hair of the face and body gradually becomes scant, and shaving is seldom or never necessary. The pubic hair tends to assume the horizontal feminine form. There is a diminution of sexual vigor, which may progress to complete loss. In women, amenorrhea is frequently the earliest symptom. The axillary hair usually becomes thin or may disappear entirely. Libido decreases or is absent.

The two sexes are about equally affected. The age incidence is earlier than that for pituitary adenomas, the greatest number of cases occurring in the second decade. Few are reported before the tenth year, probably because the growth of the tumor is usually slow. After the age of 30, the incidence rapidly decreases, although one case was reported at 57 and another at 60. The mortality with and without operation has been high.

Drowsiness was a marked symptom in the majority of cases. In a series compiled by Critchley and Ironside,⁶ it was noted in ten of fifteen cases. The excessive lethargy is apparently not related to the degree of adiposity or to the hydrocephalus found in some cases. The basal metabolic rate has not been recorded in the cases reviewed in the literature, but in my patients it was definitely subnormal. It is possible that the excessive drowsy condition so frequently observed may be indirectly due to the subnormal metabolism. No patient showed glycosuria, nor have the patients in previously recorded cases had polyuria. However, one of my patients apparently developed a temporary diabetes insipidus. Only a few determinations of the blood sugar have been recorded. These showed a low blood sugar with an increased sugar tolerance.

The changes in the ocular fundus vary with the location of the primary growth. If it develops at the angle of the infundibulum and the anterior pituitary lobe or beneath the capsule of the latter, the tumor lies below and usually in front of the optic chiasm. Growth of the tumor will, therefore, press on the under surface of the optic nerves and chiasm, producing defects in the upper quadrant of the visual fields. If the growth is most pronounced in the midportion, bitemporal hemianopsia results. Not infrequently, however, the growth tends to pass more to the right or to the left, producing left or right homonymous hemianopsia or blindness in one eye and a temporal hemianopsia in the other, depending on whether the pressure was greatest on the optic nerve behind or in front of the chiasm and on the degree of pressure on the latter. Primary optic atrophy is the rule in these suprasellar, subchiasmal lesions.

⁶ Critchley, Macdonald, and Ironside, Redvers, N. The Pituitary Adamantinomata, *Brain* 49: 437 (Dec.) 1926.

Tumors developing from the upper group of cell rests may grow first either upward or downward or equally in both directions. If the greater pressure is exerted upward, the third ventricle is early involved and partial or complete obstruction of the foramina of Monro with a corresponding degree of hydrocephalus results. Choking of the optic disks will then occur. The visual fields show simply contraction. A definite diagnosis by the changes in the disks and visual fields alone is impossible, but these taken in consideration with possible endocrine disturbances make a tentative diagnosis possible. If the roentgenogram shows calcification above the sella, then one can be certain of the location of the lesion and of its probable nature.

When the primary growth of the tumor is downward, primary optic atrophy instead of papilledema will be found. The chiasm is pushed downward and forward. Defects in the lower quadrant of the visual field appear, and finally bitemporal or homonymous hemianopsia, depending on the exact position of the downward pressure, occurs. As in the subchiasmal lesions, the process will eventually progress to total blindness unless the pressure is relieved.

Pressure upward into the third ventricle and downward on the chiasm and optic nerves usually gives a combined picture of increased intracranial pressure and primary optic atrophy with defects in the visual field. The tumors arising from the embryonic hypophyseal duct are practically the only lesions giving this combined picture. Rarely a suprasellar endothelioma may simulate the tumors of the duct, but here primary optic atrophy is generally found in one eye and choked disk in the other, probably because an endothelioma rarely occurs exactly in the midline.

The condition shown by the roentgenogram varies with the seat of the adamantinoma. When the tumor develops in apposition to the anterior hypophyseal lobe, relatively early enlargement of the sella turcica is to be expected. This may appear at first as a simple increase in size, with thinning of the sellar floor, or the anterior or posterior clinoid processes may show erosion. Actual loss of the clinoid shadows is usually noted by the time the tumor is large enough to give symptoms.

A tumor arising at the upper end of the infundibulum may show a normal sella, even when the growth has reached considerable proportions. It may, on the other hand, give a picture characteristic of a primary intrasellar tumor. This would suggest a downward prolongation of the growth into the sella, a condition which was found in one of the cases reported here. Upward growth with impingement on the third ventricle and resulting hydrocephalus may show in the roentgenogram the characteristic cranial deformities of this condition. Separation of the sutures or the presence of so-called digital markings may be noted, all indicative of increased intracranial pressure.

The most characteristic roentgen-ray observation is a suprasellar shadow. Calcification here is practically always in the wall of a cyst or of an adamantinoma, and roentgen-ray evidence is sufficient to make a diagnosis. The shadow is often crescentic in outline, suggesting the wall of the tumor. Suprasellar calcifications have been noted in a large number of adamantinomas. It was present in case 2, which is to be described later.

The presence of the tumor at operation is suggestive, but a definite diagnosis cannot be made except by microscopic examination. In the three cases in which I operated, the wall was quite firm, and definite calcification was noted in two. In the first case, a cyst containing straw-colored fluid was found. In the walls of this cyst was a dense layer of white or slightly cream-colored granular material, which was friable and appeared quite dry. The second patient presented a solid mass of similar nature, closely resembling dried sebaceous material, but on the whole considerably whiter. The third patient had a large cyst containing brownish-yellow, almost syrupy fluid, rich in cholesterol crystals. The right wall and the floor of the cyst were covered with calcareous masses, some of which resembled mother of pearl. The noncalcareous portions of the tumor were brownish yellow in contradistinction to the almost white appearance of the tumor in the first two cases.

The histologic structure varies in different parts of the same tumor, but according to Critchley and Ironside, "the presence of a single row of columnar cells, corresponding in structure to the embryonic ameloblasts, and arranged in a palisade formation at the periphery of the epithelial masses, is the criterion for diagnosing the tumor as an adamantinoma."

Ewing⁷ states

While commonly well encapsulated there may be invasion of surrounding soft tissues and bone. The main structural type is that of adenoid cystic epithelioma. In a cellular connective tissue stroma lie anastomosing masses of epithelium, the outer layers of which are cylindrical, while the inner layers become flattened and vacuolated. There is often a distinct tendency to reproduce the reticulated structure of adamantinoma, and many small cysts form in the liquefied central areas, as well as in the edematous stroma. Or squamous metaplasia is pronounced, pearls and intercellular bridges form, and keratohyaline granules appear. In some cases squamous cells are wanting, and the tumor is composed of many closely packed papillae, lined chiefly by cylindrical cells (Lewis). Either in the epithelial masses or in the walls of vessels calcific concretions may form.

Bailey⁸ settled the much disputed question regarding the presence of keratin and keratohyalin. In absolutely fresh material from three cases

⁷ Ewing, James. *Neoplastic Diseases*, Philadelphia, W. B. Saunders Company, 1922, p. 938.

⁸ Bailey, Percival. Note concerning Keratin and Keratohyalin in Tumors of the Hypophysial Duct, *Ann. Surg.* **74**: 501 (Oct.) 1921.

he was able to demonstrate keratinized cells in two and granules of keratohyalin in all three. Two of the patients had cysts containing cholesterol crystals.

The marked adiposity frequently associated with pituitary and hypophyseal duct tumors has attracted considerable clinical attention, but Warthin⁹ appears to have made the only pathologic study of the nature of these fatty deposits. He based his contribution on two cases of dyspituitarism with adiposity, in one of which the tumor was an adamantinoma. He investigated particularly the nature of the lipid contents of the liver and described a hitherto unknown type of hepatic necrosis. His conclusions are of sufficient importance to be quoted in full. He states:

In hypopituitarism there is a peculiar obesity due to infiltration of various cells of the body with a mixture of lipids—glycerin-esters and cholesterol-esters. This condition of cholesterol liposis is especially marked in the liver and adrenals, but is scattered all over the body. With deficiency of hypophysis function there appears to be associated a cholesterol retention or infiltration. Hypopituitarism must, therefore, be classed among the xanthelasmic conditions, and is related in kind to diabetic liposis and Gaucher's disease.

The hypophysis is either directly or indirectly concerned with lipid metabolism, particularly with cholesterol steatosis. Postmortem hyperpyrexia may be associated with hypopituitarism and the obesity resulting from the latter condition.

In the livers of two cases of hypopituitarism there occurred a peculiar intra-peripheral zonal necrosis unlike all previously described forms of zonal liver necrosis. Associated with this necrosis is a reparative fibroblastic proliferation, giving rise to the picture of an early intralobular cirrhosis. The relationship of this hepatic change to the hypophysis conditions remains to be shown.

It is interesting that the three cases of pituitary adamantinoma forming the basis of this report represent the two types of practically all the pathologic changes which have been noted in these cases.

The two types of endocrine disturbance are presented. The first patient was thinner than normal and would be placed in the infantile or Lorain group. The second, belonging to the Frohlich group, showed marked adiposity, especially over the hips and about the waist, and was of the type studied by Warthin. The third case did not show evidence of hypophyseal dysfunction. None of my patients were excessively drowsy at the time of admission although this seems to have been a common symptom in the cases previously reported.

The two main locations for the development of adamantinoma are represented in these patients. The patient in case 1 had an intrasellar tumor, evidently developing from the extreme lower end of the infundibular stalk. The patient in case 3 showed a similar lesion. In

9 Warthin, Aldred Scott. A Study of the Lipid Content of the Liver in Two Cases of Dyspituitarism, *J. Lab. & Clin. Med.* 2:73 (Nov.) 1916.

case 2 the patient presented a suprasellar tumor, apparently arising from the upper end of the infundibulum. The roentgen-ray evidence likewise represented the two types previously mentioned, case 1 showing enlargement of the sella turcica with destruction of the posterior clinoid processes, while cases 2 and 3 showed suprasellar calcification.

The changes in the eye also represented the two types of pathologic change in the fundus encountered in these tumors, in cases 1 and 3 primary optic atrophy was present, in case 2, choked disks.

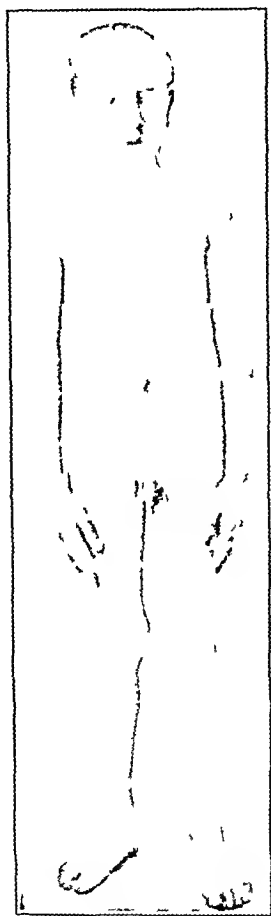


Figure 1

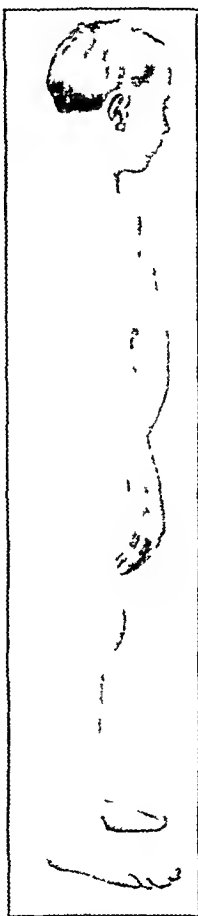


Figure 2

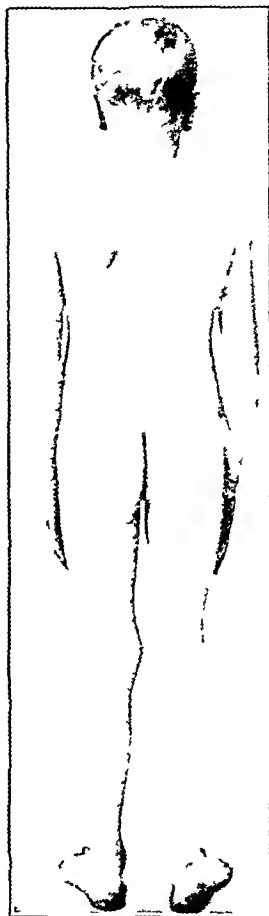


Figure 3

Fig 1 (case 1) —Normal stature, legs and arms are thin. This photograph, taken after operation, shows the absence of visible scars.

Fig 2 (case 1) —General build normal for a boy aged 9 years. The arms appear rather long.

Fig 3 (case 1) —Prominent scapulae and thin legs suggest the Lorain type of hypopituitarism.

REPORT OF CASES

CASE 1—*History*—V. W., a boy, aged 9, was admitted to the University Hospital on Nov 2, 1925, complaining of failing vision. His family history and previous personal history were normal.

Nearly a year before coming to the hospital, he had made grimaces and said there seemed to be something in his eyes. Actual visual disturbance was not apparent, however, until about five months before. At that time it was noticed that when picking strawberries he picked both the green and the red, although he did not have trouble in actually seeing the berries. This loss of color perception was not understood at first, and the boy was considered careless, until it was found by actual test that he could no longer distinguish between the two colors. With the starting of school, two months before the boy came to the hospital, actual diminution of vision was noted, and soon he was unable to read. He had not had headache, dizziness or nausea and had not vomited. The output of urine apparently had been normal.

Physical Examination—Examination showed a well proportioned boy of good stature for his age (fig 1). He was somewhat thinner than normal, but was not actually emaciated (figs 2 and 3). The head was of normal size and shape. Extra-ocular movements were normal. The pupils did not react to light, but there was slight contraction for accommodation. There was some nystagmus on

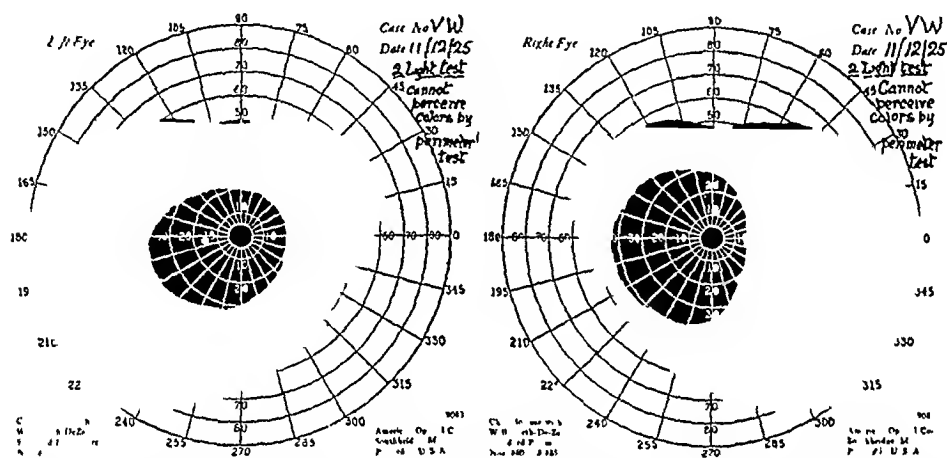


Fig 4 (case 1)—Visual fields before operation, determined by two-light tests, as vision was so reduced the regular perimeter examination could not be made. Color perception was entirely lost.

looking laterally. Tension was normal. The optic disks were pale, with a slight blurring on the right and apparent slight swelling on the left, the swelling being confined to the disk itself. The ophthalmologic report showed consecutive optic atrophy with almost complete temporal hemianopsia on the right and marked contraction of the visual field on the left. Color perception was entirely lost. The vision was so poor that examination could be made only by the two-light test (fig 4). Results of the neurologic examination, except for the changes in the eye, were negative. A roentgenogram of the skull showed a definite increase in the depth and width of the sella turcica with a thinning of its floor and destruction of the posterior clinoid processes. There were definite digital markings indicative of increased intracranial pressure (fig 5). Results of examinations of the urine and of the blood were essentially negative. A diagnosis of pituitary tumor was made, and operation was recommended.

Operation—Operation was performed on Nov 13, 1925. A large osteoplastic flap was turned downward in the right frontoparietal region. The dura was found to be under practically normal tension. The frontal lobe was elevated, and the pituitary region was approached from the frontal lateral direction.

When the region of the sella turcica was exposed, both optic nerves were found elevated and pushed laterally to either side by a tumor bulging up from the sella turcica in front of the chiasm and between the optic nerves (fig 6). This tumor was solid, except for a central area between the optic nerves, which was definitely cystic. Aspiration of this yielded a deep yellowish fluid. About 15 cc was obtained. The capsule of the tumor was then incised, and its contents were removed by a sharp curet and pituitary forceps. A considerable amount of the capsule was removed, but a portion of it on either side was firmly adherent to the carotid arteries, and this portion could not be excised. The inside of the remaining portion of the capsule was painted with Zenker's solution. The optic



Fig 5 (case 1)—Enlargement of the sella turcica and almost complete destruction of the posterior clinoid processes

nerves dropped down to their normal position. The pathologic report showed an adamantinoma, the complete description of which follows.

Pathologic Diagnosis—The diagnosis was adamantinoma, a tumor of the craniopharyngeal duct. Pituitary gland tissue was not present in the material. Microscopically, the tumor consisted of irregularly branching cords and masses of epithelial cells of the squamous cell type showing pronounced intercellular bridges and peripheral palisade arrangement. The stroma was a dense, finely fibrillated, nearly hyaline connective tissue with spindle or stellate nuclei resembling that of a tooth-bud formation. In the central portion of the larger cell masses there was a hyaline transformation of the epithelial cells into a hard, irregularly-fragmenting substance resembling an atypical enamel. In a few

areas lime-salts had been deposited in this. The fracture was irregularly conchoidal. The blood supply was fairly abundant, in the form of irregular sinusoidal spaces and dilated capillaries in the youngest stroma. The neoplasm was precisely like the adamantinomas of the jaw and was interpreted as a pituitary adamantinoma originating in the cranio-pharyngeal duct, slowly replacing the sella turcica and pituitary gland by pressure atrophy and exerting pressure



Fig 6 (case 1)—Intrasellar adamantinoma with central cyst. There is marked pressure on the optic nerves and chiasm.

on the optic chiasm. Its malignancy was only of local growth and pressure, there was no danger of metastasis—A. S. Warthin (figs 7, 8, 9).

Convalescence and Recovery—Convalescence was satisfactory. The patient's visual acuity was greatly improved, and within a week after operation he could see a fine thread. Roughly tested, there was a slight early improvement in the visual fields. Reexamination on Feb 24, 1926, showed a progression of the optic atrophy in the left eye, so that on that date there was no color perception.

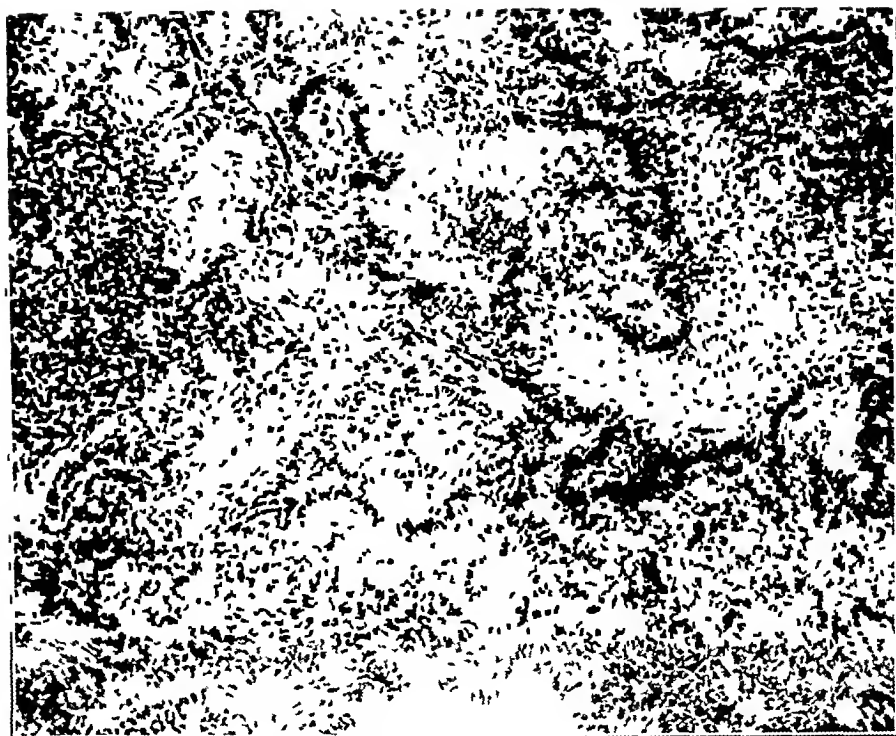


Fig 7 (case 1) —Adamantinoma of the cranio-pharyngeal duct. Solid masses of prickle cell epithelium with peripheral palisade arrangement. No hyaline change is present in this area except at the lower part of the section.



Fig 8 (case 1) —Adamantinoma of the cranio-pharyngeal duct. Hyaline degeneration (atypical enamel formation) of epithelial masses. Palisade arrangement of the basal layer of epithelial masses, producing a pseudo gland-like appearance.

The right eye showed marked improvement in the form fields, and blue and red were now recognizable in a small segment on the nasal side (fig 10). He continued to develop normally after the operation. In January, 1927, it was reported that he was showing signs of diabetes insipidus and desired to drink large quantities of water and passed a correspondingly increased amount. We recommended daily injections of pituitary extract. His physician reported that he tried 0.5 cc a day hypodermically and later increased the dose to 1 cc, but apparently it did not cause any diminution in the urinary output. A later report giving actual measured intake and output showed that this was not excessive for a boy of his age. Whether he had had a temporary diabetes insipidus is questionable, but at the time of the final report there was no evidence of it.

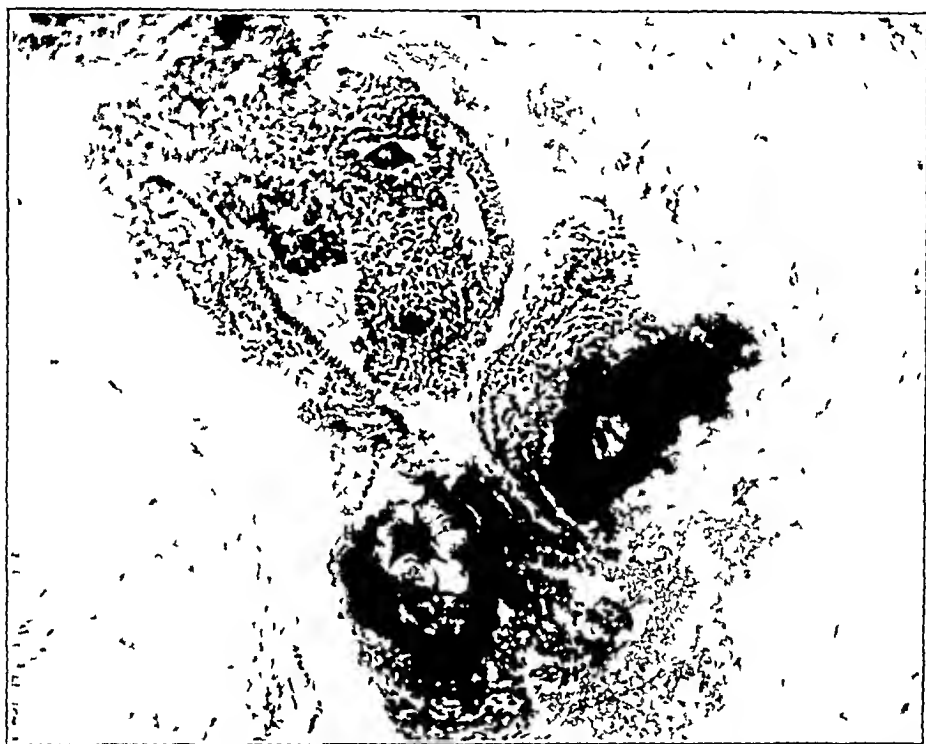


Fig 9 (case 1)—Calcification of atypical enamel masses formed by prickle cell epithelium, adamantinoma of the cranio-pharyngeal duct

CASE 2—History—M. M., a girl, aged 10, was admitted to the University Hospital on Nov 17, 1926, because of rapidly failing vision. Her previous history was essentially negative. She had walked and talked at the age of 1 year. Her mental and physical growth had proceeded normally, except for the development of excessive adiposity. The present illness had started one year before, with severe headaches, nausea and vomiting when she awoke in the morning. She was usually relieved by noon. Headaches and vomiting continued at intervals of about ten days until six weeks before admission, since which time she had remained free from these symptoms. Appendectomy had been performed in the hope of relieving the nausea and vomiting, but without benefit. Her vision was tested in January, 1926, and glasses were prescribed. No lesion of the fundus was noted. For some time she had noticed that her vision was failing, and her parents had noticed a rapid loss of vision during the two weeks preceding admission. The patient said that her vision had been poor

and steadily failing for some weeks, but she did not tell her parents, as she did not wish to worry them. Recently the loss of vision had been rapid, as evidenced by her ability on admission to count fingers held before her at a distance of three feet, but four days later she could no longer count fingers even when they were held close to her face. Her appetite and intake of water had not been unusual.

Physical and Neurologic Examinations—The patient was generally obese, with excessive deposits of fat above the hips and around the waist (figs 11 and 12). The head was of normal contour. The cranial nerves, with the exception of the optic, were normal. The neck, thorax, abdomen and extremities were normal. All reflexes were present and equal. There was no disturbance in sensation. Examination of the fundus showed a rather marked optic atrophy with papilledema in both eyes. In the right eye, the choked disk measured 3 diopters, in the left, from 4 to 5 diopters. The pupils reacted to light and in accommodation. The visual fields showed complete loss of color perception in both eyes. On the left, a small area for white was preserved in the temporal field, on the right, only a small area in the central nasal field was present (fig 13).

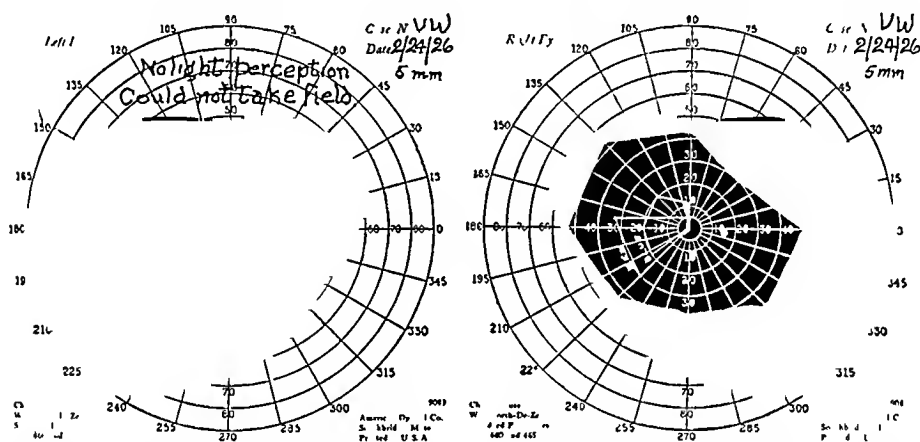


Fig 10 (case 1)—Visual fields taken two months after operation. There is marked improvement in the form field in the right eye, examination being made with the standard perimeter. Color perception for blue and red has returned in a small area in the right nasal field. In the left eye the optic atrophy present before operation has progressed to complete atrophy with loss of light perception.

Basal metabolism tests showed minus 15 per cent (Du Bois standard), minus 16 per cent (Talbot standard), with a pulse rate of 84. Glucose tolerance fasting, 0.095, one-half hour after taking 17 Gm of glucose per kilogram of body weight, 0.174, one and one-half hour period, 0.094, two and one-half hour period, 0.094. Results of examination of the urine were negative. Examination of the blood revealed hemoglobin, 82 per cent, red corpuscles, 3,520,000, white corpuscles, 7,600. Differential blood count polymorphonuclears, 34 per cent, lymphocytes, 61 per cent, basophils, 0 per cent, eosinophils, 3.5 per cent, transitional cells, 2.5 per cent.

The roentgenogram of the head showed definite digital markings indicative of prolonged intracranial pressure. The sella was only slightly enlarged, but the anterior clinoid processes were much thinner than normal, and the posterior clinoid processes were apparently completely destroyed. Above the sella was an irregularly calcified mass, roughly circular in outline and suggesting calcification in the wall of a suprasellar cyst (fig 14).

The diagnosis made was suprasellar cyst, evidently pressing upward on the third ventricle, thereby interfering with the flow of cerebrospinal fluid with resulting choked disks and probably beginning hydrocephalus. It also pressed downward, possibly causing a primary optic atrophy and symptoms of hypopituitarism, as evidenced by the excessive adiposity, the low basal rate and the increased sugar tolerance. Operation with an approach to the tumor from above the sella offered the only means of relief.

Operation—Operation was performed on Nov 22, 1926. A large osteoplastic flap was turned downward from the right frontoparietal region. The dura was

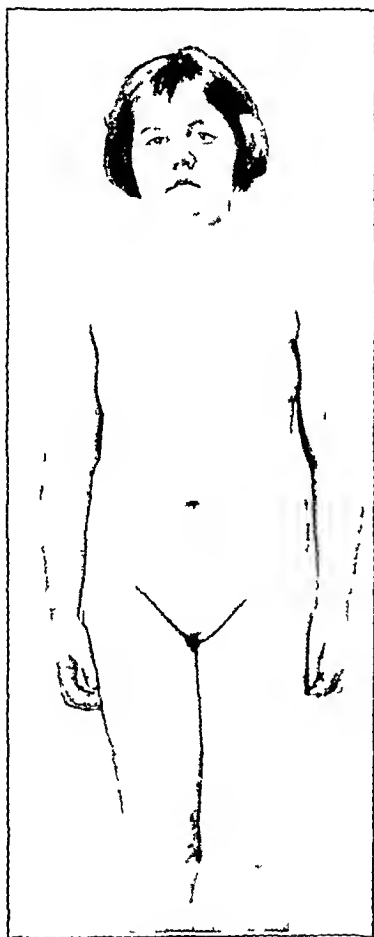


Figure 11

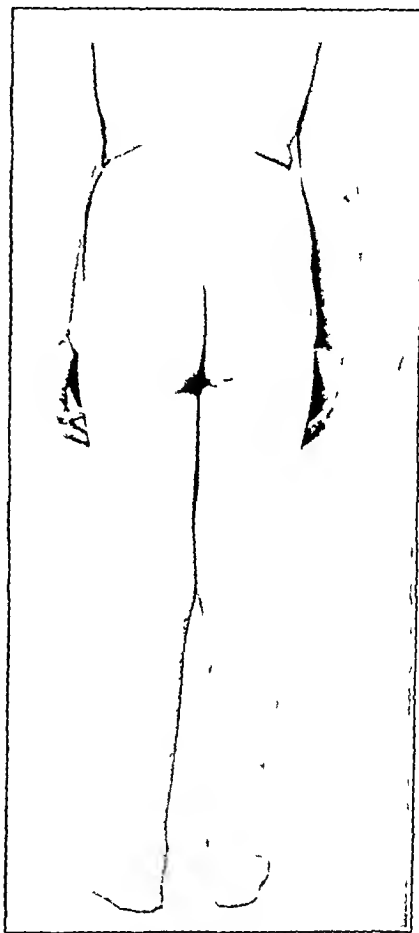


Figure 12

Fig 11 (case 2)—Marked adiposity, especially above the hips and around the waist. Apparent mammary development is due entirely to fat.

Fig 12 (case 2)—The excessive deposits of fat above the hips and around the waist are well shown.

under considerable tension. This was relieved by tapping the dilated right lateral ventricle with the evacuation of a large amount of clear cerebrospinal fluid. The dura was opened widely, the base of the flap being placed near the midline. In spite of the complete relief of pressure afforded by evacuation of the ventricle, it was difficult to elevate the median inferior surface of the frontal lobe. This was due to the fact that the tumor extended well up into the third ventricle. The right and left optic nerves and the chiasm were, however,

exposed without difficulty. There was no tumor in the anterior portion of the sella turcica, but one could see the diaphragm of the sella pushed sharply downward. The diaphragm was thin, and the pituitary, as viewed through the diaphragm, appeared normal. The brain was elevated posterior to the chiasm, which later had been pushed downward and forward by the tumor occupying the region of the floor of the third ventricle. This tumor extended downward posterior to the posterior clinoid process, thus passing in front of the pons, and a tongue also passed anteriorly into the posterior part of the sella, elevating the posterior edge of the chiasm and pushing the whole chiasm sharply forward and downward. The capsule of the tumor was opened posterior to the chiasm, and a slightly calcified wall was found. Within the wall of this cyst a dry, whitish, sebaceous-appearing material was packed tightly. Hair was not present. The dry, rather hard tumor mass was removed with a curet. Much of the capsule of the tumor immediately posterior to the chiasm and that portion passing into the sella was removed. Some of the capsule was rather firmly adherent to the under side of the optic tracts and of the chiasm. When an attempt was

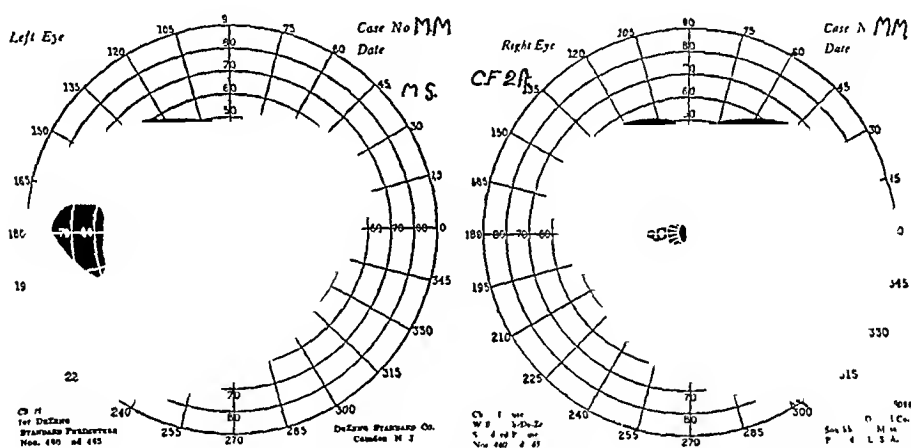


Fig 13 (case 2)—Visual fields, color perception was entirely lost. There is complete right homonymous hemianopsia and extreme contraction of form fields on the left. Fingers could be counted at a distance of two feet.

made to remove the capsule posterior to the posterior clinoid process, the patient suddenly became pulseless, and it was necessary to cease further attempts to remove the tumor, how much remained in the region of the third ventricle was not determined. The dura was closed, the osteoplastic flap returned to position, and the scalp closed in layers.

A transfusion of blood was given immediately, and the pulse showed marked improvement, but the patient died about three hours later. Autopsy was refused.

The exact cause of the sudden collapse was not clear. Up to the minute the pulse became imperceptible it had been of good quality, with a rate of 126 and a blood pressure of from 108 to 100 systolic and from 78 to 76 diastolic. Appreciable bleeding did not occur at any time. The operation confirmed the pre-operative conception, the tumor having pushed upward the floor of the third ventricle with resulting hydrocephalus. It had also pressed the optic chiasm forward and downward. The tumor, however, proved to be solid rather than cystic.

Pathologic Diagnosis—A tumor of the craniopharyngeal duct of the type of an adamantinocarcinoma was found. In part, it was infiltrating an atypical



Fig 14 (case 2) —The sella turcica is somewhat enlarged and the posterior clinoid processes are practically destroyed. Above the sella can be seen a calcified mass in the wall of the adamantinoma. Digital markings, indicative of increased intracranial pressure, are present.

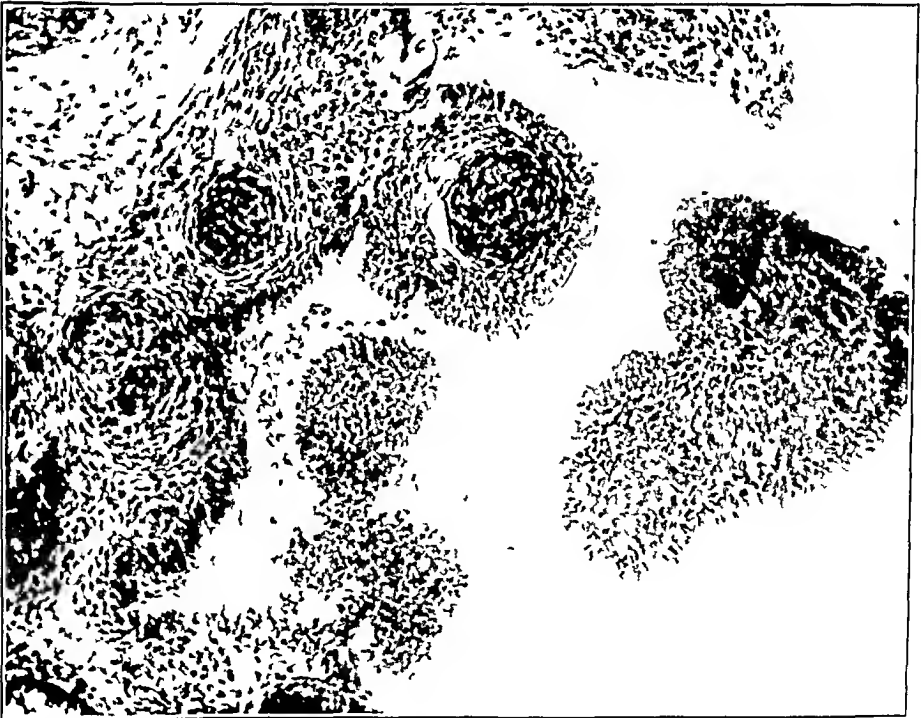


Fig 15 (case 2) —Tooth-bud-like growth of prickle cell epithelium with palisade peripheral arrangement, adamantinocarcinoma of the craniopharyngeal duct.



Fig 16 (case 2)—Adamantinocarcinoma of the craniopharyngeal duct
Tooth-bud-like epithelium formations infiltrating the brain Higher magnification
of conditions shown in figure 15

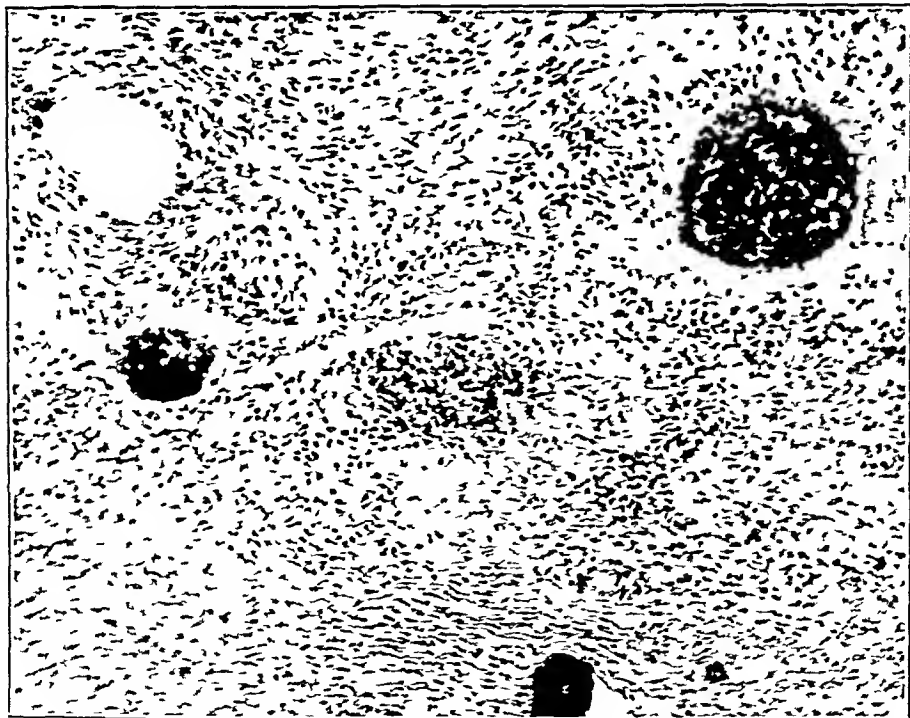


Fig 17 (case 2)—Infiltration of brain tissue by adamantinocarcinoma of the
craniopharyngeal duct In the upper part on the left is a cord of tumor cells
showing enamel transformation or prickle cell epithelium at the bottom is a
calcified cord Four different stages of growth of a tumor are represented in the
photomicrograph

neuroglia Throughout the growth there were numerous pink-staining hyaline masses, probably representing an atypical enamel formation, and many of these were calcified—C V Weller

Pathologic Description—The microscopic appearances of this tumor were identical with those of the growth in case 1, with the exception that this one showed a greater degree of differentiation and some degree of infiltration into the adjacent brain tissue and meninges It consisted of cords and masses of prickle cell squamous epithelium showing peripheral palisade arrangement, a dentine-like stroma and a central peculiar hyaline transformation of the epithelial cells into conchoidally-fragmenting dense hyaline material showing a strong affinity for lime salts, leading to the production of irregularly nodular, extremely hard concretions These appearances were interpreted as representing an atypical enamel formation The structure of the tumor was identical with that of the adamantinomas of the jaw, it represented a more advanced stage than that in case 1 and exhibited a greater degree of local malignancy (infiltration and pressure atrophy) Its malignancy was local only, and metastases were not to be expected It was interpreted as a developmental disturbance of the cranio-pharyngeal duct, representing abortive tooth-bud formation, giving rise to cell masses of enamel-organ type, and it was, therefore, classed with the adamantinomas No remains of the pituitary gland were present Frohlich's syndrome would probably have developed—(A S Warthin)

CASE 3—*History*—R B, a girl, aged 6, was admitted to the University Hospital, Sept 8, 1927, complaining of headaches and failing vision The past history was unimportant She began to talk and walk at 1 year of age The body and mental growth had been regular and normal She had not had any contagious diseases The family history was negative for any endocrine disturbances

In August, 1926, she developed marked conjunctivitis with profuse lacrimation, which her physician diagnosed as "hay-fever" However, she was drowsy, and for three days could be aroused for only a minute or so at a time These symptoms disappeared in about two weeks, following which she was free from symptoms until the first of February, 1927 She then developed a severe headache and in two or three hours vomited profusely The headache, which was referred to the left posterior parietal region, persisted, however, and seemed to increase in severity The tonsils were removed the last of February in the hopes of controlling the headache, but without relief She again became drowsy She complained of pain in the eyes, especially in the presence of a bright light Headaches in the left posterior parietal region continued for three months, during which time she was confined to bed She was then free from symptoms and was as active as any normal child until August, 1927, when the headache reappeared but in the right posterior parietal region The pain was not constant as before, occurring only two or three times a day She usually awakened in the morning crying from the headache Sometimes the pain lasted for only a few minutes and generally disappeared suddenly She lost her appetite and complained, 'I have a nasty taste in my mouth' At one time she likened this taste to that of rotten eggs Her eyes were then examined for possible cause of the headache Optic atrophy was found in the left eye, and glasses were prescribed The headaches persisted, and a month later she entered the University Hospital There had not been any nausea or vomiting since the attack in February The weight had remained normal and polydipsia or polyuria had not been noted

Physical Examination—The patient was well developed and normally proportioned for her age (fig 18). She was not adipose and did not have any abnormal local deposits of fat. The head was of normal size and configuration (figs 19 and 20). The cracked-pot sound was not present. Movements of the eyes were normal in all directions. The pupils were equal and contracted to light and in accommodation. Ophthalmoscopic examination showed primary optic atrophy involving the entire left disk and beginning in the nasal half of the right disk. Perception of light was present only in the left eye. The form field in the right eye was confined to the nasal half. Vision in this area was apparently normal.



Figure 18



Figure 19



Figure 20

Fig 18 (case 3)—Normal configuration in a child of 6. There is neither thinness as in case 1 nor adiposity as in case 2. The head is of normal shape and size.

Fig 19 (case 3)—Normal development of body. The protuberant abdomen is not due to fat but to poor posture.

Fig 20 (case 3)—No evidence of hypopituitarism in contrast to cases 1 and 2. The skin is soft and of fine texture. The hair of the head is abundant.

The neurologic examination was normal. Physical examination of the thorax, abdomen and extremities did not disclose any abnormalities. The child was alert and apparently normal mentally.

Roentgen-ray examination showed an enlargement of the sella tursica with some destruction of the posterior clinoid processes. A calcified shadow was



Fig 24 (case 3) —Area showing structure of adamantinoma Appearance of squamous epithelium with intercellular bridges, slight palisade arrangement and large masses of laminated, dense epithelial hyaline transformation, showing calcification Atypical enamel formation

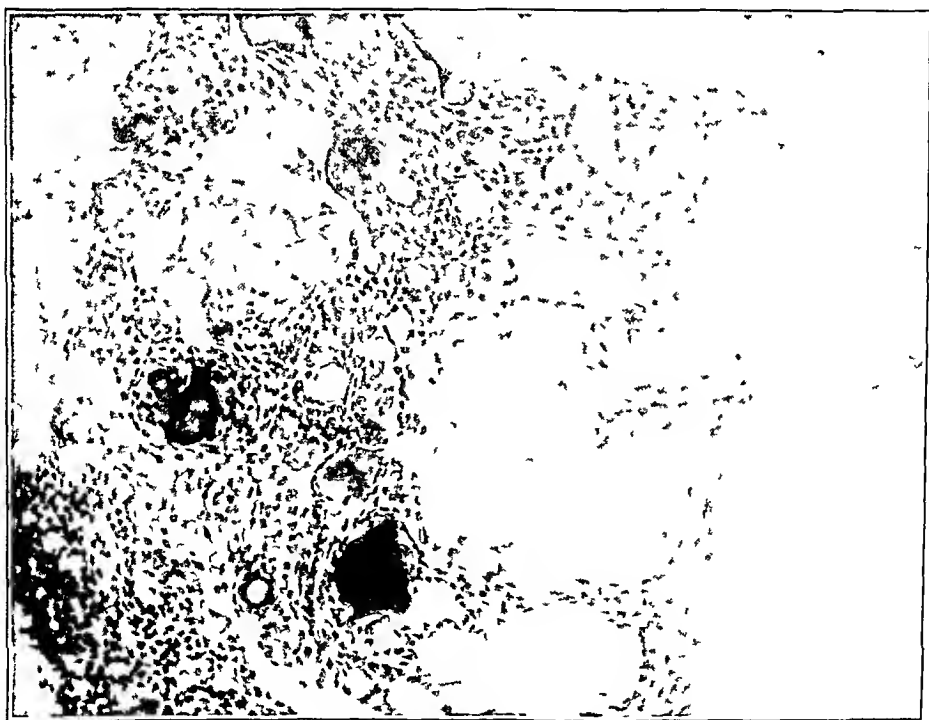


Fig 25 (case 3) —High power appearance of figure 24, showing the epithelial hyaline transformation of squamous cell epithelium with intercellular bridges Formation of atypical enamel from epithelium The palisade arrangement does not show in this field

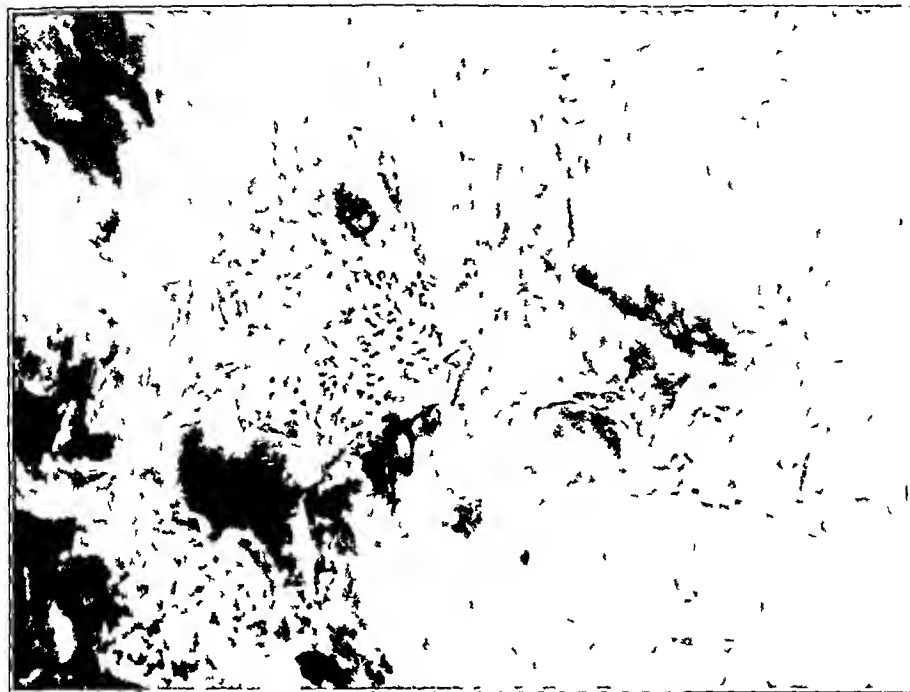


Fig 26 (case 3) —High power appearance of atypical enamel formation, showing laminated structure and conchoidal cleavage. Lime salt deposits in enamel masses are shown.



Fig 27 (case 3) —Postoperative appearance, showing absence of calcification in sella and suprasellar region. The silver clips placed on the dura are considerably magnified, since they are on the side of the head opposite the film.

Similar masses of solid material containing concretions, some of which resembled pearl, covered the floor of the cyst. After its contents were evacuated, the entire cyst wall was removed. Due to the elevation of the chiasm and the partial destruction of the posterior clinoid processes, it was possible to see the anterior surface of the pons and the basilar artery. Both optic nerves had been markedly stretched by the tumor; the right was uniformly thinned, the left, while much flattened throughout its course, appeared nearly divided just distal to the chiasm. Neither nerve was injured during the operation. A small, flattened plaque, apparently the remains of the pituitary gland, remained on the floor of the sella turcica. The dura was sutured, the osteoplastic flap returned to position and the incision closed in layers. The child's condition at the completion of the operation was excellent.

Pathologic Diagnosis (C. S. Warthin).—The condition was diagnosed as a typical adamantinoma of the cranopharyngeal duct and a cyst in a Rathke's pouch with cholesteatoma. The cyst was lined in part by squamous epithelium, in part by columnary epithelium. Some of the squamous epithelium showed intercellular bridges. This is a more complex disturbance of the cranopharyngeal duct, as it contains areas of different tissues.

Pathologic Description (C. V. Weller).—The material removed presented varying appearances in different portions. Certain areas, apparently capsular portions of the mass, showed a dense connective tissue through which were scattered cords and small masses of epithelial cells which showed a distinct peripheral palisade arrangement. Small cystic structures were also present, some of which showed a squamous epithelial lining. In other areas there were dense granular and coarsely laminated or pseudoprismatic masses staining pink with eosin, except in those areas in which they were partially infiltrated by lime salts. Many of these masses had a distinct conchoidal fracture and were found in association with prickle celled epithelium in a matrix of looser, somewhat myxomatous connective tissue. Areas of secondary degeneration and old hemorrhage were represented by deposits of cholesterol and much phagocytized blood pigment. The structure was therefore that of a disturbance of development of the cranopharyngeal duct with typical areas of adamantinoma and much formation of enamel.

Convalescence and Recovery.—Convalescence was rapid and without incident. Within twenty-four hours after the operation the child was able to count fingers with the left eye, although previously only perception of light was present. This return was confined to the central vision. The nasal field on the right remained normal, the temporal field seemed slightly increased. A roentgenogram of the sella turcica showed that all the calcareous material had been removed (fig. 27).

The child returned to the hospital for examination one month after the operation. The general condition was excellent. Vision in the left eye was still confined to the central field, but there was definite improvement in the right. The nasal vision remained normal, and about 30 degrees of temporal vision had been regained. While at home she had shown moderate polydipsia and polyuria, but this was growing less. Measurements of intake and output had not been made, but a frequency had been noted in her desire to drink and to urinate. When she was examined, it was found that this tendency was so slight that the administration of pituitary was not considered necessary.

SUMMARY

Three cases of adamantinomas in the pituitary region are reported. The first patient was possibly thinner than normal and might be placed in the Lorain group. The second presented a typical Frohlich syndrome of excessive adiposity and low rate of basal metabolism. The third belonged in the rare group having an intrasellar adamantinoma with normal basal metabolism and sugar tolerance and without any physical evidence of dyspituitarism. The two tumors illustrate two of the locations in which adamantinomas may develop in the primary region. The first and third cases were primarily intrasellar and the tumor undoubtedly arose in the extreme lower end of the infundibular stalk. In the second the tumor arose from the extreme upper end of the infundibulum. In the first and third primary optic atrophy was present, in the second, choking of the optic disk with optic atrophy and definite hydrocephalus, due to blockage of the third ventricle.

A tentative diagnosis of a pituitary adamantinoma should be easily made, although the symptoms vary with the location and size of the tumor. The majority of patients present the Frohlich syndrome of dystrophia adiposo-genitalis. In a child with this syndrome, with simple excessive adiposity, or a marked increase in weight, the possibility of a pituitary adamantinoma should immediately be suspected. A few patients, however, show unusual slenderness. Occasionally the physical development is normal.

Excessive drowsiness is a common symptom. Headache, nausea and vomiting may or may not be present, depending on the presence of increased intracranial pressure. Visual disturbances have been noted in every case, usually a slow, progressive loss with bitemporal or homonymous hemianopsia. The presence of primary optic atrophy or of papilledema depends on the location of the tumor.

The roentgen ray offers a valuable means of diagnosis. The sella turcica is usually enlarged, and the anterior and posterior clinoid processes are thinned or completely destroyed. In many cases calcification above the sella turcica is shown, and this definitely indicates the presence of a cyst or tumor. In many of these the lesion is undoubtedly a pituitary or hypophyseal duct adamantinoma.

Operation is always indicated, as no other treatment can give relief. While there is considerable difference of opinion as to the choice of operative procedures in true pituitary tumors, I believe that adamantinomas are best approached from above. Certainly when the tumor has originated above the sella turcica as in case 2, no other approach is feasible.

The prognosis is extremely grave, as a review of the literature indicates, although early operation may prolong life with adequate vision for an indefinite period. In a few cases it is undoubtedly possible to remove the tumor completely, as in case 3. The early diagnosis of a pituitary adamantinoma followed by early operation will materially increase this number and will at least conserve vision in those who cannot be cured.

POSTOPERATIVE MASSIVE ATELECTASIS

I THE INFLUENCE OF POSTURE

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ROCHESTER, N Y

AND

JAMES J JOELSON, M D

CLEVELAND

The number of reported cases of massive atelectasis has been multiplied in the last few years. The spectacular clinical picture of the fully developed unilateral condition is now familiar. It occurs as a postoperative complication, following trauma, and associated with spontaneous painful diseases both intrathoracic and outside the chest. The importance of the atelectatic process in other types of postoperative pulmonary complications and in the bilateral form has not been clearly elucidated, but judging from the meager data available along these lines, it appears to be great. An explanation of the origin of postoperative massive atelectasis, therefore, will undoubtedly do far more than solve this clinical mystery, since it may prove to be a most important step in reducing the incidence of those fatal postoperative pulmonary complications now classified as pneumonia.

In spite of careful investigation, the original cause of postoperative massive atelectasis has not been proved. The discussion of its etiology is still in the realm of hypothesis, and in this paper we do not hope to be able to establish its ultimate etiology. However, all new observations in regard to the mechanism of massive atelectasis are valuable, and it is our purpose to report such data.

Harrington¹ remarked, in reporting a case, that the postoperative posture of the patient has received scant consideration in the literature on massive atelectasis. Briscoe² is alone in attributing the chief rôle in the etiology of this complication to the recumbency of the patient. His point of view was based on the observation of relative deflation of the bases of both lungs as the result of "prolonged quiet breathing in the supine position in such people as do not use the abdominal muscles to

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1 Harrington, S W. Relief of Postoperative Massive Collapse of the Lung by Bronchoscopic Aspiration, *Ann Surg* **85** 152 (Jan) 1927.

2 Briscoe, J C. The Mechanism of Postoperative Massive Collapse of the Lung. *Quart J Med* **13** 293 (April) 1920.

fix their chests" This can be dismissed as the explanation of postoperative massive atelectasis for two reasons (a) Such conditions obtain in most laparotomies, while the incidence of massive atelectasis is about 1 per cent, and (b) it offers no basis for the most significant manifestation of the complication, viz, displacement of the mediastinum Several writers mention the interference with respiration arising from recumbency as having a secondary influence on the development of the condition (Bradford,³ Hirschboeck,⁴ Eades⁵) In all these cases the flat recumbent posture alone is considered The only reference to the possible significance of a unilateral position in the development of postoperative massive atelectasis is the allusion of Harrington¹ Tidy⁶ explained the contralateral collapse associated with nonpenetrating wounds of the opposite thoracic wall as being due to the patient's lying on the well side and thus splinting its respiratory movements Webb, Forster and Gilbert⁷ have shown that if a normal person lies continuously on one side, there is marked displacement of the mediastinum and opacity of the lung on the dependent side Such an effect, however, quickly disappears when the person turns on his back and takes a deep breath Consequently, this resembles the relative airlessness at the bases of the lungs described by Briscoe,² and is entirely dissimilar to the clinical manifestations of unilateral massive atelectasis

THE INFLUENCE OF POSTURE

Our interest in the influence of posture in the development of massive atelectasis was awakened by the following unusual case

CASE 1—*History*—J M, a Greek, aged 24, was admitted to the Lakeside Hospital on Feb 22, 1925, complaining of abdominal pain His family history was good He had never had any respiratory symptoms or diseases

The present illness started ten years before, when the patient began to have recurring attacks of abdominal pain, which extended to either or both lumbar regions and to the back The pain was severe and colicky, and would usually last for several hours In addition to the pain, the patient also had frequency of micturition and nocturia Hematuria did not appear until about six years after the onset of the attacks of pain, but it had recurred frequently since then At

3 Bradford, J R Massive Collapse of the Lung as a Result of Gunshot Wounds, with Especial Reference to Wounds of the Chest, *Quart J Med* **12** 127 (Oct) 1918, (Jan) 1919

4 Hirschboeck, F J Postoperative Massive Collapse of the Lungs, *Am J M Sc* **164** 268 (Aug) 1922

5 Eades, M F Postoperative Massive Atelectasis Report of Cases, *Boston M & S J* **195** 258 (Aug 5) 1926

6 Tidy, H L Acute Lobar Collapse of the Lung, *Lancet* **1** 1245, 1914

7 Webb, G B, Forster A M, and Gilbert, G B Postural Rest for Pulmonary Tuberculosis, *J A M A* **76** 846 (March 26) 1921

the onset of the present illness the attacks came on about once every three months, but they became steadily more severe and more frequent

Physical Examination—The patient was small but fairly well developed. The heart and lungs were normal. The results of the remainder of the physical examination were negative, except for slight tenderness in the left lumbar region.

Laboratory Observations—The urine was cloudy and acid; its specific gravity was 1.015. The tests for albumin and for sugar were negative and the microscopic examination showed numerous pus cells. The phenolsulphonphthalein test showed that 55 per cent of the dye was excreted in two hours and ten minutes. The blood urea was 25 mg per hundred cubic centimeters. The blood Wassermann reaction was negative.

Roentgenograms of the urinary tract showed shadows which were suggestive of renal calculi in the region of each kidney. On the right side there was a single large shadow, on the left side, both a large and a small shadow were present.

Cystoscopic examinations were made without general anesthesia. A moderate degree of cystitis was present. The urine from both kidneys showed numerous pus cells, and *Bacillus coli* was cultured from each specimen. One cubic centimeter of phenolsulphonphthalein was given intravenously. The dye appeared from the right kidney in four minutes and from the left in five minutes. The right kidney excreted 25 per cent of the dye in fifteen minutes, while the left excreted only 10 per cent in the same length of time. Pyelograms showed a large calculus in the pelvis of each kidney and also a small calculus in a lower calyx of the left kidney. The pelves were of normal size and shape.

Operation and Course—On February 28, a left pyelotomy was done under nitrous oxide-oxygen and ether anesthesia. The patient was placed on his right side, and the usual position for an operation on the kidney was obtained by means of a "kidney elevator." An oblique lumbar incision was made, the kidney was freed and delivered, the posterior wall of the pelvis was opened and the stone was extracted. The time of the procedure was somewhat lengthened because it was necessary to take roentgenograms of the delivered kidney to localize the smaller stone which was in one of the minor calyces. A small incision was made through the renal parenchyma in the attempt to locate this stone. The pelvic incision was approximated with interrupted sutures of fine catgut, and the wound was closed in the usual way with drainage of the renal fossa. The duration of the anesthesia was two hours, of which the actual operation consumed one hour and twenty minutes. There was nothing unusual about the induction of anesthesia, its subsequent course or the period of recovery. The patient's condition and color remained good throughout the entire procedure.

The patient made a good immediate recovery from the operation. Toward evening, however, his temperature began to rise, and by midnight it had reached 39.8 C. The pulse rate was 112, but the respirations remained about 22 per minute.

The next morning (March 1) the patient presented the classic picture of postoperative massive atelectasis of the right lung. The temperature was 39.4 C, the pulse rate, 140, and respirations 40. There was no cough, thoracic pain or sputum. The accessory muscles of respiration were being used, and the respirations were frequent and shallow. On inspection of the chest a striking asymmetry was evident. The anterior surface of the right side of the chest from the clavicle down to the fourth rib was flattened and moved only slightly with respiration while the same region of the left side of the chest showed a wide



Fig 1 (case 1) —Roentgenogram made on March 2, 1925, forty-eight hours after the first operation, a left pyelotomy. It shows a shadow of increased density in the right upper pulmonary field which has a concave lower margin and in which the pulmonary markings cannot be recognized. Below this the illumination is less impaired. The trachea and heart are displaced markedly to the right, and the right side of the diaphragm is unduly high. The left pulmonary field is translucent. The appearance is that of a postoperative massive atelectasis, largely if not entirely, confined to the right upper lobe.



Fig 2 (case 1) —Roentgenogram made on March 4, 1925, two days after (figure 1) showing the right upper pulmonary field a little less dense and the right lower pulmonary field much more dense than on the previous examination. The heart and trachea are still displaced to the right. The outline of the right margin of the heart and the right portion of the diaphragm cannot be identified. The left pulmonary field is normal. The appearance suggests that the lower portion of the lung is now more involved than it was, whereas the upper portion is less involved.

respiratory excursion. The vigor of movement was strikingly different on the two sides, that of the right second, third and fourth ribs being much diminished. The right costal margin moved through a greater lateral excursion than the left. The cardiac pulsation was visible 3 cm to the right of the sternum in the second and third intercostal spaces. The upper border of hepatic flatness was at the fourth rib in the midclavicular line, and none was present in the epigastrium. The right apex was retracted, and there was dullness of the entire right lung anteriorly, most marked over the right upper lobe. In the right lower mid-axillary region, moderate tympany was present. Bronchial breathing was heard over the right apex posteriorly down to the level of the angle of the scapula, but rales were not noted. The left lung was hyper-resonant, and the breath sounds were of normal quality, but exaggerated. The left border of the heart was percussed in the fifth intercostal space 5 cm to the left of the midline. When the patient was tested with 0.5 cc of epinephrine hydrochloride, he was found

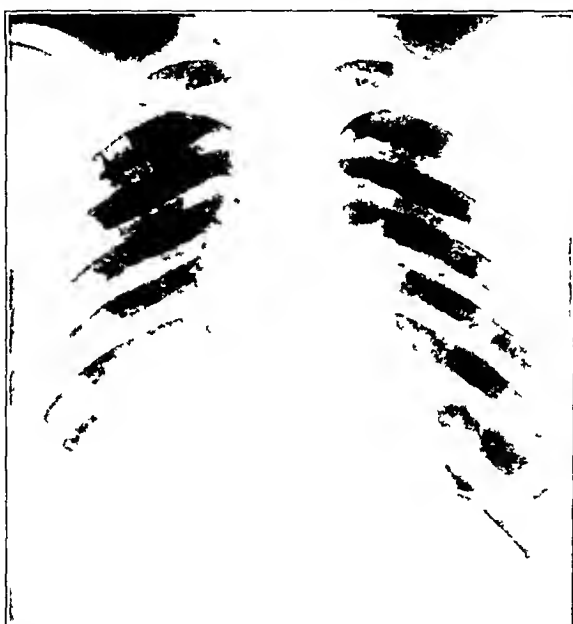


Fig. 3 (case 1)—Roentgenogram made on March 24, 1925, showing the chest normal except in the right lower pulmonary field where some increase in density and heavy pulmonary markings still persist.

to have a definite hypersensitivity. The epinephrine hydrochloride did not produce any change in his pulmonary condition.

On March 2 (second day after operation), the temperature was still elevated between 38.2 C (100.8 F) and 39.8 C (103.6 F), and the respirations were still rapid, but less than on the previous day. The heart and mediastinum were markedly displaced to the right (figs. 1 and 2). Dullness was present over the entire right lung, but rales were not heard.

On March 3 (third day after operation), the patient's condition was about the same, but, in addition, he began to cough and to expectorate a small amount of yellow, tenacious sputum.

This condition continued for one week, then the temperature came down to 38 C (100.4 F), and the cardiac dullness began to approach the midline. The cough and expectoration remained slight. The improvement continued, and within three weeks after the operation, the condition of the chest had returned to practically normal (fig. 3).

The patient was discharged from the hospital twenty-five days after the operation, and was told to return in about two months for removal of the calculus in the right kidney

Second Operation—On May 14, the patient was readmitted to the hospital for pyelotomy on the right side. He had been well, except for one attack of renal colic on the right side. He had not had any respiratory symptoms, and physical examination of the chest did not disclose any abnormalities of the heart or lungs.

Roentgenograms of the kidneys showed the calculus in the right one to be the same as on previous examinations.

A right pyelotomy was done on May 16, under nitrous oxide-oxygen and ether anesthesia. The patient was placed on his left side, and the usual position for an operation on the kidney was obtained by means of a "kidney elevator." An oblique lumbar incision was made, the posterior renal surface was freed, and the pelvis was exposed without delivering the kidney. A small longitudinal incision was made through the posterior wall of the pelvis, through which the stone was



Fig. 4 (case 1)—Roentgenogram made on May 18, 1925, forty-eight hours after the second operation, a right pyelotomy. It shows a shadow of increased density occupying the entire left pulmonary field. The heart and trachea are displaced to the left. The outlines of the left margin of the heart and the left portion of the diaphragm are obliterated, but from the position of intestinal gas shadows it is evident that this side of the diaphragm is at least as high as the right. The right pulmonary field is translucent. The appearance is that of an extensive postoperative atelectasis of the left lung.

easily removed. The wound was closed in the usual way, with drainage. The total duration of the anesthesia was one hour and twenty-five minutes, whereas the operation itself lasted one hour. The anesthesia was taken well, and the patient's color and condition remained good throughout the entire procedure.

On May 17 (first day after operation), the patient's temperature rose to 39.6 C (103.3 F), the pulse rate was 120, the respirations were 40 and a slight cough was present. The precordial activity was marked to the left of the sternum, and the apex beat was located 1 cm to the left of the left nipple line. The respiratory movements of the upper part of the left side of the chest were

decreased. Dulness was present over the base of the left lung posteriorly, and the breath sounds were absent. Some scattered sibilant rales were heard over the remainder of the left lung.

On the next day (May 18), the patient showed definite evidence of a post-operative massive atelectasis of the left lung. The temperature was 40 C (104 F), the pulse rate, 120, and the respirations, 40. Slight cyanosis was present. The cardiac activity was marked to the left of the sternum, and the apex beat was 3 cm outside the left nipple line in the fourth intercostal space. The respiratory movements of the left side of the chest were more diminished, and the dulness at the base of the left lung was more marked. The breath sounds were absent over the left base and distant over the remainder of the left side of the chest (fig 4).

These symptoms and signs gradually disappeared, and nineteen days after the operation the patient's temperature, pulse rate and respirations were normal, and the examination of the chest did not reveal any abnormalities. The patient was

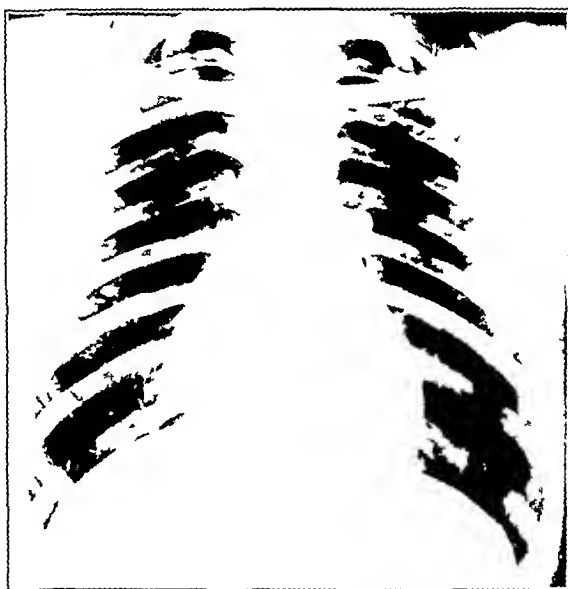


Fig 5 (case 1)—Roentgenogram made on Oct 8, 1925, showing essentially normal pulmonary fields except for a slight increase in density of the right base and unduly heavy pulmonary markings along the right border of the heart.

discharged on June 10 (twenty-five days after operation) feeling well and in good condition. He has been seen regularly in the follow-up clinic since then. He has not had any respiratory symptoms, and repeated examinations of the chest have not revealed any abnormalities of the heart or lungs (fig 5).

Although we had found that the patient showed a positive reaction to the hypersensitivity test with epinephrine hydrochloride at the time of his first massive atelectasis, we wanted to discover whether he would show the same reaction when his condition was uncomplicated. Therefore, on June 28, 1927, the hypersensitivity test with epinephrine hydrochloride was repeated, and the reaction was again definitely positive (fig 6).

In this case there are several points of interest that will be discussed later. The most obvious fact is that following a separate operation on each kidney the patient developed massive atelectasis of the opposite

lung Not only during the operation on the kidney was the position of the patient such that the contralateral lung was dependent, but the lumbar wound resulted in his remaining at least partially turned on the opposite side during the immediate postoperative interval in which the massive atelectasis developed This raised the question whether there might be a correlation between the posture of the patient and the side on which localization of the massive atelectasis occurred

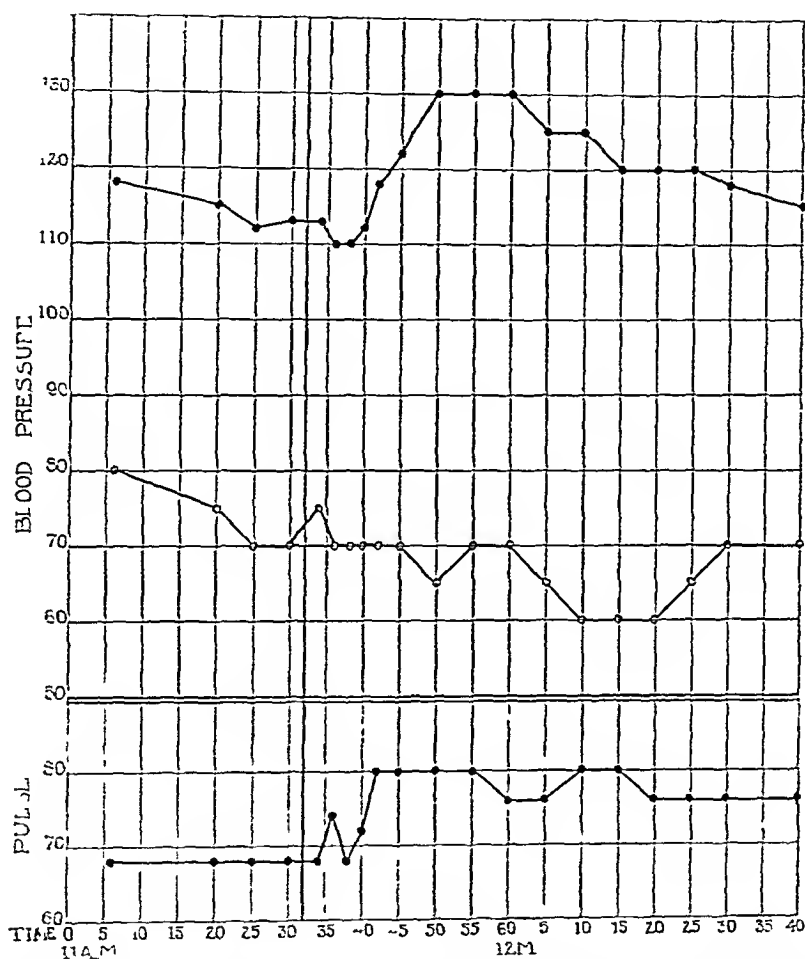


Fig 6 (case 1) —Test of hypersensitivity to epinephrine hydrochloride made on June 28, 1927 After control readings of the pulse rate and blood pressure were obtained (with the patient recumbent and quiet) 0.5 cc of a 1:1,000 solution of epinephrine hydrochloride was injected subcutaneously at 11:32 a. m. There was a sustained increase in both pulse rate and blood pressure but no nervous manifestations. The patient was quiet throughout the procedure and dozed off to sleep at 12:50 p. m. Interpretation: Definitely positive, though not extreme, hypersensitivity to epinephrine hydrochloride.

In order to determine this point our series of twenty-two cases of postoperative massive atelectasis studied by one or both of us in the last four years was analyzed for the factor of posture. In most cases, the character of the operation did not necessitate lying on one side.

In two instances, however, this condition was fulfilled. Summaries of these two cases are as follows:

CASE 2—P. J. S., an American, aged 28, was admitted to the Peter Bent Brigham Hospital, Boston, April 16, 1923, on account of dysuria of five years duration, which was associated with hematuria and frequency of micturition. Two years after the onset of these symptoms, a typical attack of renal colic occurred on the left side and lasted several days.

The patient said that he had not had any symptoms of respiratory or cardiac disease. Physical examination gave negative results, and the chest was normal.

Cystoscopic and roentgenologic examinations revealed a moderate sized vesical calculus and a smaller calculus in the pelvis of the left kidney.

On April 18, a pyelotomy on the left side and a suprapubic cystotomy were done by Dr. Quimby under nitrous oxide-oxygen anesthesia. The patient was first placed on his right side in the usual position for an operation on the left



Fig. 7 (case 2)—Roentgenogram of chest made one week after a left pyelotomy, showing a diffuse mottling of the entire right lung with decreased aeration, flattening of the right side of the thorax, a high position of the diaphragm on the right side and displacement of the heart and trachea toward the right side.

kidney. After the kidney was freed and delivered, the stone was removed through an incision in the posterior wall of the renal pelvis. The wound was closed in the usual manner, with drainage. The patient was then returned to a dorsal recumbent position. Cystotomy and removal of a vesical calculus were performed, and the wound was closed in layers, the bladder being drained by an indwelling catheter in the urethra. The operation and anesthesia were uncomplicated. The following day the patient's temperature, pulse rate and respiratory rate mounted and the second day after the operation definite signs of a postoperative pulmonary complication were noted, with marked dulness and bronchial breathing over the right middle and lower lobes, but no râles. The displacement of the heart to the right was not found by physical examination but was demonstrated by the roentgenogram (fig. 7).

The patient made a good recovery from the postoperative massive atelectasis. Within eleven days after operation the temperature, pulse rate and respirations were normal, and five days later, the pulmonary signs had disappeared, a roentgenogram of the chest at this time was normal except for an accentuation in the pulmonary markings of the right lower lobe.

The patient was discharged from the hospital nineteen days after the operation, feeling well. A follow-up letter from the patient four years after his operation stated that he had not had any respiratory symptoms or diseases or urinary symptoms.

CASE 3—E. B., a man, aged 26, was admitted to the Rochester General Hospital, Sept. 10, 1926, complaining of pain in the right sacro-iliac joint.

The results of physical examination were negative, except for tenderness over the right sacro-iliac joint. The chest was normal.

Fusion of the right sacro-iliac joint was performed by Dr. E. W. Phillips on September 11. Nothing unusual was noted in the postoperative convalescence until September 18, one week after operation, when the patient complained of cough and pain on the left side of the chest. Examination showed flattening and restricted motion in this part of the chest, flatness and diminished breath sounds at the base and a friction rub in the left axilla. Roentgen-ray examination proved the condition to be a massive collapse of the left lung. The complication did not influence the patient's convalescence from the operation.

COMMENT

These were the only cases observed by us in which massive atelectasis developed after an operation that required the patient to lie on one side. It can be seen that such conditions occur only with a limited number of operations, chiefly those on the kidney and on the sacro-iliac joint.

A search of the literature has added five more instances. Lihenthal⁸ refers to a case reported by Hahn⁹ in which a typical massive atelectasis developed on the left side two days after a nephrectomy on the right side for hypernephroma. The second case reported by Jackson and Lee¹⁰ was that of a boy, aged 12, who was kept lying on his right side after laparotomy for an appendical abscess. On the third day after operation, he developed massive atelectasis of the right lung. Hunt¹¹ reports the case of a patient with a ruptured duodenal ulcer who was kept turned on the right side after operation in order to facilitate drainage. He developed a massive atelectasis on the

8 Lihenthal, H. *Thoracic Surgery*, Philadelphia and London, W. B. Saunders Company, 1926, vol. 2, p. 86.

9 Hahn, L. J. *Massive Collapse of the Lung Following Nephrectomy*, *Internat. J. Med. & Surg.* **37**: 232, 1924.

10 Jackson, C. and Lee, W. E. *Acute Massive Collapse of the Lungs, Discussion of its Mechanism and of Its Relation to Foreign Bodies in Bronchi and Postoperative Complications*, *Ann. Surg.* **82**: 364 (Sept.) 1925.

11 Hunt, E. L. *Massive Atelectasis of Lung as Surgical Complication* (case 1), *Boston M. & S. J.* **194**: 58 (Jan. 14) 1926.

dependent side viz the right Harrington¹ recorded a case of massive atelectasis on the left side which occurred the day after a nephrectomy was performed on the right side Finally Sante's¹ second patient presented a total massive atelectasis of the left side which was diagnosed seven days after a nephropexy was done on the right side

If our own cases are added to those in the literature massive atelectasis has been seen nine times following operations that necessitate the patient's lying on his side as shown in the table In each instance the collapse occurred in the dependent lung The evidence that this is not merely a coincidence is stronger for two facts (1) in seven of the nine cases, the atelectasis occurred on the side contralateral to operation whereas the homolateral lung is ordinarily the one involved (2) in the majority the collapse was on the left side which

Total Cases of Massive Atelectasis Following Operations Which Necessitated the Patient's Lying on One Side, Including the Author's Cases and Those Reported in the Literature

Case	Operation	Dependent Lung	Side of Atelectasis
Case 1 first operation	Left pyelotomy	Right	Right
Case 1 second operation	Right pyelotomy	Left	Left
Case 2	Left pyelotomy and cystotomy	Right	Right
Case 3	Right sacro-iliac fusion	Left	Left
Harrington's case	Right nephrectomy	Left	Left
Jackson and Lee's case 2	Laparotomy with drainage for appendiceal abscess	Right	Right
Hunt's case 1	Laparotomy with drainage for ruptured duodenal ulcer	Right	Right
Harrington's case	Right nephrectomy	Left	Left
Sante's case 2	Right nephrectomy	Left	Left

is the side much less commonly involved in postoperative cases We therefore feel justified in concluding that when the patient has been consistently lying on one side, if unilateral massive atelectasis develops, it will occur in the dependent lung

In most instances the patient was turned on one side both during the operation and in the postoperative period while the complication was developing Consequently these data do not present definite proof as to whether the effective time interval of such a postural influence is during or after the operation, or at both times

ETIOLOGIC CONSIDERATIONS

The posture of the patient under such circumstances appears to determine the localization of the complication It is however certainly not the primary cause of massive atelectasis The simple fact that atelectasis follows only a small minority of the operations on the kidney

¹² Sante L R Massive (Atelectatic) Collapse of the Lung with Especial Reference to Treatment I A M A 88 1539 (May 14) 1927

is ample evidence that there is a more fundamental factor than the position of the patient alone. From a study of the physical aspects of the condition, it is evident that there must be an obstruction at some point in the respiratory tract. The displacement of the mediastinum demonstrates an initial difference in the pressures on the two sides of this structure as conclusively as a tambour in the laboratory would show it. Certainly, this pressure would be equalized by the movement of air rather than by the great displacement of the mediastinum, if the air passage were freely open. Theoretically, this displacement of the mediastinum could be caused by an obstruction in the distended lung with an acute emphysema. The free movement, in fact the exaggerated respiratory excursion of the opposite lung, and the diminished or absent excursion of the atelectatic lung are sufficient proof that the obstruction of the air passages is on the side toward which the mediastinum is displaced. Up to this point, the evidence appears conclusive. The mechanism of unilateral postoperative massive atelectasis must include obstruction to the free exchange of air in the involved lung. Final proof of the cause and the location of this obstruction is lacking.

It is our belief that the fundamental condition which initiates massive atelectasis is a nervous reflex which affects both lungs and probably occurs frequently in a minor degree. This is suggested by many facts. In the first place, the occurrence of massive atelectasis following operations under local anesthesia and its association with trauma or spontaneous painful disease, even when the lesion is at a distance from the lung (Sante, case 1), bespeak its initiation through either the nervous or the vascular system. In the second place, as Scrimger¹³ and Scott¹⁴ have previously suggested, the number of persons with neurogenic stigmas in the group who develop postoperative massive atelectasis is apparently disproportionate. The hypersensitiveness to epinephrine hydrochloride shown by the few patients tested falls in line also with an autonomic imbalance in these persons. In the third place, our case 1 is the second one recorded in which massive atelectasis has occurred in the same patient, after successive operations. Farris¹⁵ reported the first instance of such a case. The latter patient developed massive atelectasis on the right side after an operation for omental adhesions. A second laparotomy was necessary two months later, and again the operation was followed by massive atelectasis of the

13 Scrimger, F. A. C. Postoperative Massive Collapse of Lung, *Surg Gynec Obst* **32** 486 (June) 1921

14 Scott, W. J. M. Postoperative Massive Collapse of the Lung, *Arch Surg* **10** 73 (Jan) 1925

15 Farris, H. A. Atelectasis of Lung (case 7), *Canad M A J* **15** 808 (Aug) 1925

right lung. Such cases illustrate the susceptibility of certain persons to postoperative massive atelectasis.

Perhaps the most important factor in guiding our opinion toward the reflex nature of the underlying etiologic agent was the reaction of the lung to operation, as manifested by auscultation. Our attention was first called to the rapid variation in sibilant and sonorous râles which may be heard in cases of massive atelectasis. This was described in a previous paper¹⁴ (cases 38 and 39). Since then we have noticed it in several other instances. At some time, more commonly during the developmental period of the condition, whistling râles and squeaks much like those in an asthmatic attack were heard. These were often scattered through both sides of the chest, although they were usually more prominent in the affected side. In some instances, within half an hour or even during the same examination these sibilant râles almost entirely disappeared, but during a later examination they were again loud throughout the chest. The changes were not associated with any expectoration or moist râles during this period. Our interpretation of the rapid appearance and disappearance of sibilant râles was that in both lungs the lumina of the finer air passages were undergoing variations in size, resulting from alterations in bronchomotor or vasomotor tone. After observing this phenomenon in definite cases of massive atelectasis, we desired to determine whether evidence of such a reflex could be obtained in uncomplicated postoperative cases. Three patients with inguinal hernia, operated on under local anesthesia, were carefully examined before and after operation. In two of the three, sibilant râles developed at times and were heard over both lungs posteriorly. These râles also appeared and disappeared. They were much less pronounced than those in cases of atelectasis, but they were of a similar character and did not resemble the crepitant râles heard over the edge of the lung when it expands on the deepening of respiration. The râles were heard best from twenty-four to thirty-six hours after operation. Similar râles were not caused merely by recumbency without operation. It was our impression, then, that a simple operation under local anesthesia (at least in some cases) had caused a bilateral reflex narrowing of the smaller air passages. It is extremely difficult to get absolute proof of this action, but such an hypothesis seems to offer the best explanation of the clinical observations.

If the primary causative agency in the production of massive atelectasis is a bilateral reflex, how is the usual striking unilateral form of the condition produced? The answer to this question is twofold. First, perhaps the more common form of this condition is not the massive unilateral atelectasis, but the less extensive bilateral condition. Evidence that the latter is an important and serious postoperative pulmonary complication is gradually accumulating, although it is much

more difficult to diagnose clinically than the unilateral type (Bergamini and Shepard¹⁶ and Hirschboeck⁴) It may be that most of the conditions now diagnosed as postoperative bronchopneumonia will be found to arise as bilateral lobular atelectatic areas, just as unilateral massive atelectasis was not until recently differentiated from postoperative pneumonia In the second place, while the initiating reflex condition is bilateral, unless the obstruction of the air passages in a part of the lung becomes complete or acts as a reverse check valve (thus, allowing air to pass out of, but not into, the lung), massive atelectasis in its recognized unilateral clinical form will not occur Undoubtedly, there are secondary factors which influence the completeness of the obstruction One of these, we believe that we have demonstrated to be a continued unilateral posture of the patient If massive atelectasis occurs, the dependency of one lung for some reason causes the localization of the process in this side The mechanism that causes this localization has not been demonstrated The initial reflex is probably vasodilative in character The most striking histologic feature found post mortem in massive atelectasis is an extreme pulmonary congestion, almost an angiomatous condition (Bradford,³ Santee,¹⁷ and Bergamini and Shepard¹⁶) This is probably the one outstanding difference in the lung between postoperative massive atelectasis and pulmonary collapse caused by the pressure of a hydrothorax or pneumothorax Quite possibly, obstruction becomes complete on the dependent side in massive atelectasis because of greater congestion in the dilated pulmonary capillaries By whatever method posture induces localization of the atelectasis, however, it may play a rôle even in patients who are placed on their backs It is much easier for most patients to roll on their right side after laparotomy, especially after the more common incisions on the right side of the abdomen In a former paper¹⁴ (figs 5 and 6, 1925), the position that these patients with massive atelectasis assume for comfort was illustrated It was presented to show why the asymmetry of the chest and of the respiratory excursion was not at once obvious. It is possible, however, that this position, which may mask detection of the condition and which is assumed for comfort, may also be responsible for the localization of the pulmonary lesion The cases of contralateral collapse which were extremely common following wounds of the chest (Crymble¹⁸) may well be examples of this suggestion that a

16 Bergamini, H, and Shepard, L A Bilateral Atelectasis (Massive Collapse) of Lung, *Ann Surg* **86** 35 (July) 1927

17 Santee, H E Bilateral Massive Collapse of Lung, *Ann Surg* **85** 608 (April) 1927

18 Crymble, P T Gunshot Wounds of the Chest *Brit J Surg* **5** 363 (Jan) 1918

unilateral posture determines the localization of atelectasis in the dependent lung

An obvious corollary to this idea of the influence of posture is that after operation the patient should not be allowed to remain constantly in one position. He should be turned from side to side so that the dependency of one lung does not occur, particularly during the immediate postoperative period.

Undoubtedly, other secondary factors besides posture greatly hasten the completion of the obstruction of the smaller air passages. Jackson and Lee have particularly stressed the secretion of a thick tenacious mucus. This is probably one of the most important elements in the completion of the obstruction, although we feel that the obstruction is in the small peripheral air passages rather than in the main bronchi. A diminution in the respiratory force may be another important factor.

When, by these processes, a major portion of one lung is shut off from respiratory exchange, it soon becomes atelectatic, and a compensatory factor affects the process in the remaining lung. It is a common observation that as the respiratory excursion of the atelectatic lung diminishes, that of the other lung increases. In our opinion, this is due to a compensatory hyperventilation of this lung which, in spite of the initial bilateral pulmonary reflex, prevents the development of any serious obstruction in the small respiratory passages of the second side.

Our conception of the development of unilateral massive atelectasis is, then, as follows: 1 Initial pulmonary reflex, (probably vasomotor) causes bilateral partial obstruction in the peripheral respiratory passages. 2 Secondary factors, such as position and tenacious secretion, make this obstruction complete on one side in advance of the other. 3 When this occurs on one side compensatory hyperventilation of the other side keeps these latter respiratory passages open (should this not occur, bilateral atelectasis is produced). 4 The air on the side of the bronchiolar occlusion is absorbed within a few hours (or more rarely may possibly be exhausted by a reverse check-valve obstruction (Jackson and Lee¹⁹), and the complete picture of a unilateral massive atelectasis develops.

SUMMARY

1 A case is reported in which contralateral postoperative pulmonary massive atelectasis developed after separate successive operations on each kidney.

2 Nine instances of unilateral massive atelectasis have been assembled in which the patient had been lying consistently on one side. The posture of the patient seemed to determine the localization of the condition which was uniformly in the dependent lung.

¹⁹ Jackson and Lee (footnote 10 p. 386)

3 Observations are presented favoring the view that the initial etiologic factor in massive atelectasis is a nervous reflex affecting both lungs. Secondary factors then determine the unilateral localization.

NOTE—Since writing this article we have learned of direct measurements of the intrapleural pressure in massive atelectasis by Elkin.²⁰ These express numerically the greater negative intrathoracic pressure on the atelectatic side which is shown qualitatively by the displacement of the mediastinum.

20 Elkin, Dan C. *Ann Surg*, in press

DISTRIBUTION OF THE SYMPATHETIC RAMI TO THE BRACHIAL PLEXUS

ITS RELATION TO SYMPATHECTOMY AFFECTING THE
UPPER EXTREMITY *

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ST LOUIS

Excision of the stellate ganglion or section of the gray rami which connect this ganglion with the brachial plexus has become a recognized surgical procedure, especially in diseases involving the blood vessels of the upper extremity. The aim of this procedure in diseases of the blood vessels is vasomotor denervation of the extremity. Excision of the stellate ganglion alone, or section of the gray rami which connect it with the brachial plexus, however, does not completely eliminate the sympathetic nerves of the upper limb in a large percentage of cases. The operation has failed to produce the desired results in certain cases, probably because of incomplete sympathetic denervation of the blood vessels which were involved.

During the progress of studies involving the gray rami associated with the brachial plexus and the distribution of sympathetic fibers in the upper extremity, my attention was called to the inconstant intra-thoracic ramus that connects the first and second thoracic nerves as a possible pathway through which sympathetic fibers that leave the sympathetic trunk below the stellate ganglion might enter the first thoracic nerve and become incorporated in nerves arising from the brachial plexus. Accordingly, the present study of the lower cervical and upper thoracic portions of the sympathetic trunks and the communicating rami joining the spinal nerves which contribute to the innervation of the upper extremity was undertaken in order to obtain more exact knowledge regarding the sources of the sympathetic innervation of the upper limb and, if possible, to afford a rational basis for an operative procedure that will in all cases effectively deprive the blood vessels of this limb of their vasomotor nerves.

The chief sources of sympathetic fibers to the upper extremity are the middle cervical and stellate ganglions. These ganglions, as well as the upper thoracic sympathetic ganglions are extremely variable. Not infrequently the middle cervical ganglion is absent. When it is present, it is generally located about the level of the body of the sixth cervical vertebra. It is usually connected through the gray rami with the fifth

* From the St. Louis University School of Medicine

and sixth cervical nerves, in some instances, also with the fourth and seventh cervical nerves (Potts, 1925)¹ In some instances the middle cervical ganglion lies close to the stellate ganglion. In such cases, the communicating rami arising from the cervical sympathetic trunk may join the fifth and sixth and possibly the fourth and seventh cervical nerves.

A discrete, inferior, cervical sympathetic ganglion occurs but rarely, if at all, in man. This ganglion commonly fuses with the first thoracic sympathetic ganglion to form a stellate ganglion. In some instances the second thoracic sympathetic ganglion is also incorporated in the stellate ganglion. This ganglion varies greatly in size and form. It commonly lies about the level of the neck of the first rib, but it may occupy a somewhat lower position. Gray rami arising from the stellate ganglion join the seventh and eighth cervical and the first thoracic nerves. Not infrequently, especially if the middle cervical ganglion is absent, a gray ramus from the stellate ganglion joins the sixth cervical nerve. At times the stellate ganglion sends a gray ramus to the second thoracic nerve. The first thoracic nerve also sends a white ramus into the stellate ganglion.

Although an intrathoracic ramus of the second thoracic nerve joins the first thoracic nerve in a large percentage of cases, the second thoracic nerve is not commonly regarded as contributory to the brachial plexus. In forty-eight cadavers examined during the present study, an intrathoracic ramus connecting the first and second thoracic nerves was present bilaterally in twenty-one and unilaterally in nine. In the twenty-one cadavers in which it was present bilaterally, this ramus was described as large in ten, of medium size in seven and as small in four. In the nine cadavers in which it was present on only one side, it was described as of medium size in five and as small in four.

According to statements in the textbooks regarding this inconstant ramus of the second thoracic nerve, it may join only the intercostal ramus of the first thoracic nerve or only the brachial plexus, or it may contribute fibers to both the first intercostal nerve and the brachial plexus. In the cadavers examined in the present study, this ramus joined the first intercostal nerve distal to its origin from the first thoracic nerve in only six cases, in all of which it was described as medium or small. In all the other cases it joined the first thoracic nerve proximal to the origin of the first intercostal nerve. If the ramus in question is small, all of its fibers may still be incorporated in the first intercostal nerve, although a contribution of fibers from the second thoracic nerve to the brachial plexus is not precluded. Not infrequently

1 Potts, T. K. The Main Peripheral Connections of the Human Sympathetic Nervous System, *J. Anat.* 59: 129, 1925.

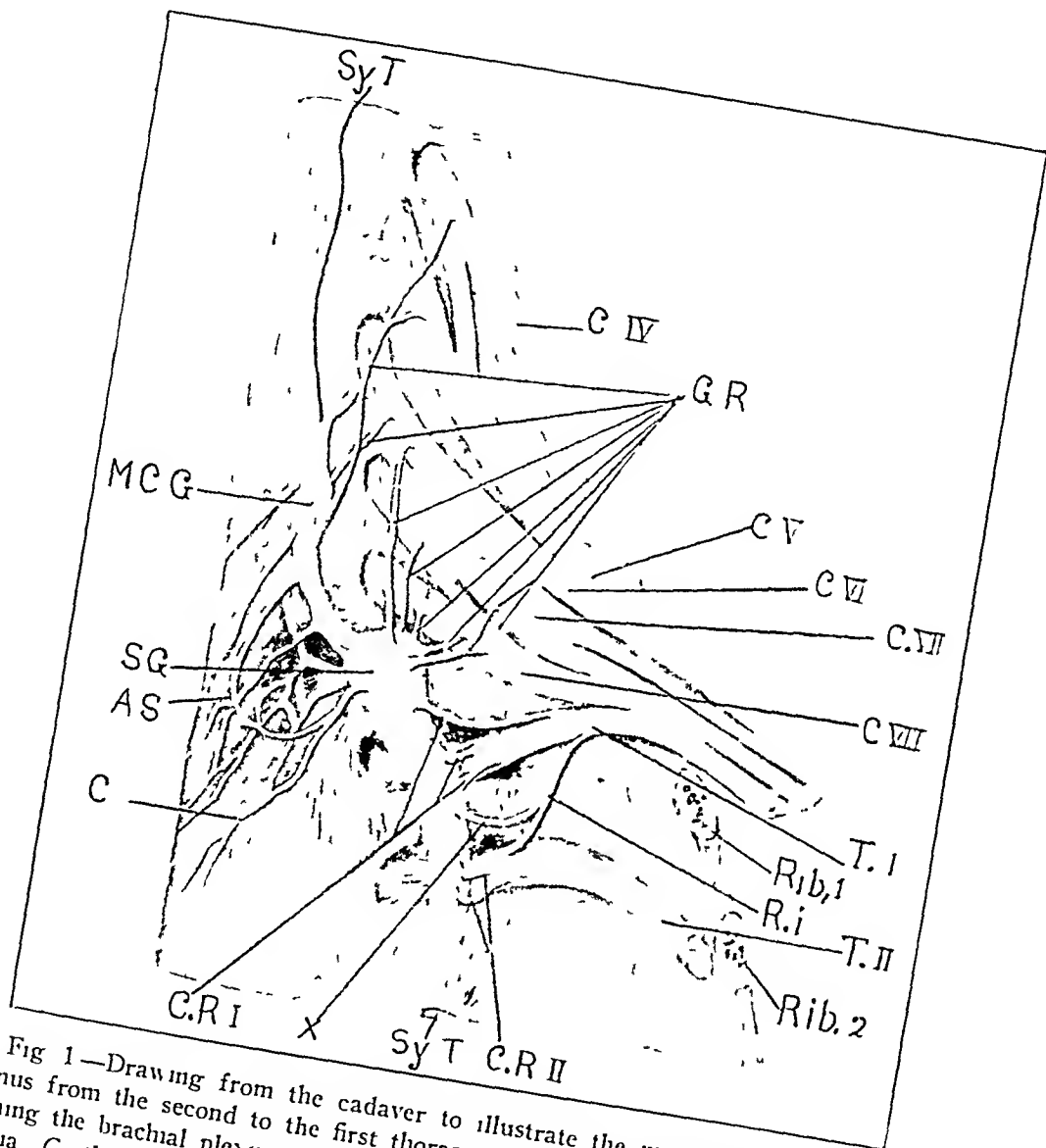


Fig 1—Drawing from the cadaver to illustrate the inconstant intrathoracic ramus from the second to the first thoracic nerve and the communicating ramus joining the brachial plexus. In the illustrations, *A S* indicates the innervation of the clavicle, *C*, the cardiac nerves, *C IV* to *C VIII*, cervical nerves, *C R I* communicating ramus to first thoracic nerve, *C R II*, communicating ramus to second thoracic nerve, *G R* gray communicating ramus to cervical nerves, *M C G* middle cervical ganglion, *R*, inconstant intrathoracic ramus from second to first thoracic nerve, *S G*, stellate ganglion, *S₁ T*, sympathetic trunk, *S*, sympathetic ramus joining the ramus from the second to the first thoracic nerve, *T II*, second thoracic nerve, *I I*, first thoracic nerve.

this ramus is actually larger than the first intercostal nerve. In such instances, the second thoracic nerve clearly contributes fibers to the brachial plexus.

The second thoracic nerve is commonly connected with the second thoracic sympathetic ganglion or the sympathetic trunk by a white and a gray ramus. In some of the cases in the present study, a gray ramus from the second thoracic sympathetic ganglion or the sympathetic trunk

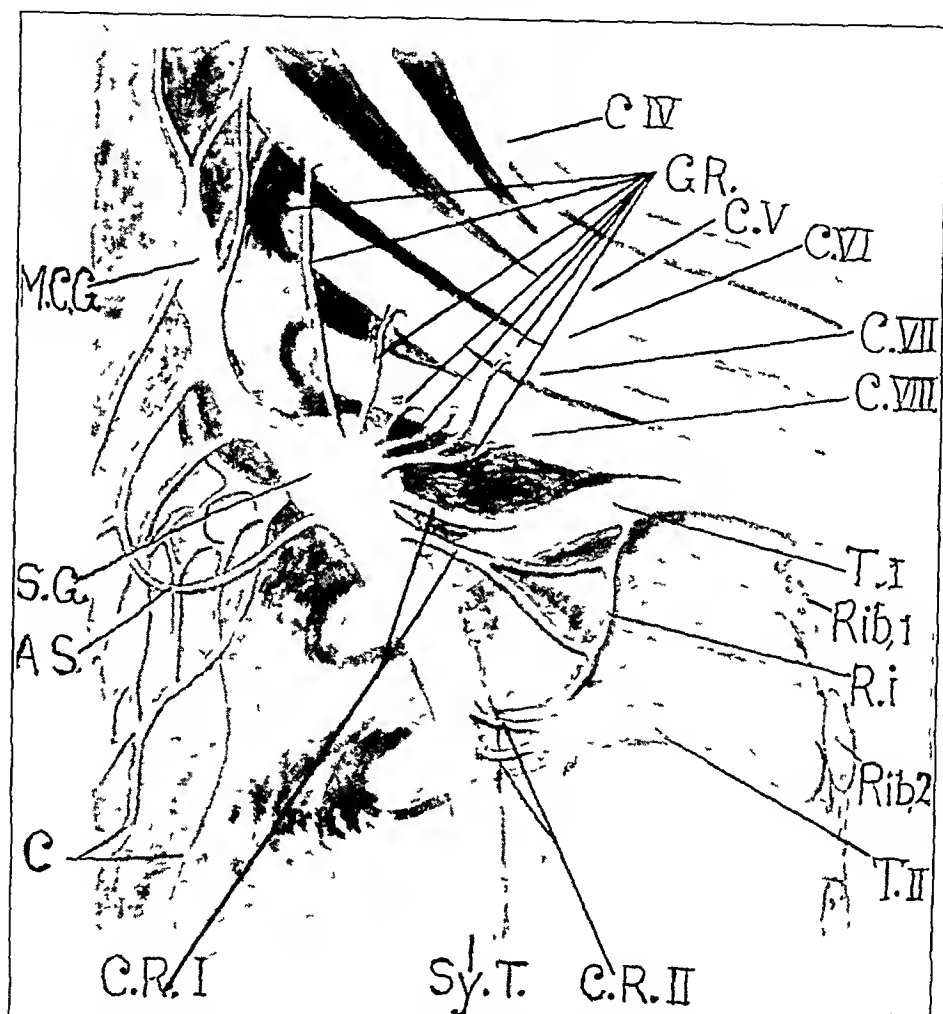


Fig. 2—Drawing from the cadaver to illustrate variation in the inconstant intrathoracic ramus from the second to the first thoracic nerve.

trunk was traced directly into the ramus connecting the first and second thoracic nerves (fig. 1 a). In other cases a ramus from the stellate ganglion was also traced into this ramus. In all cases in which a gray ramus was traced from the second thoracic ganglion or the sympathetic trunk directly into the ramus joining the first thoracic nerve, one or more communicating rami also joined the second thoracic nerve. Not infrequently, a communicating ramus joined the second

thoracic nerve at or near the point of origin of the ramus that joins the first thoracic nerve. Sometimes it was apparent that some of the fibers in the communicating ramus joined the ramus leading to the first thoracic nerve. In a few instances, a small ramus was traced into the first thoracic nerve directly from the second thoracic sympathetic ganglion or the communicating ramus connecting this ganglion with the second thoracic nerve. Figure 3 illustrates a large intrathoracic ramus that arises from the second thoracic nerve farther distally than usual,

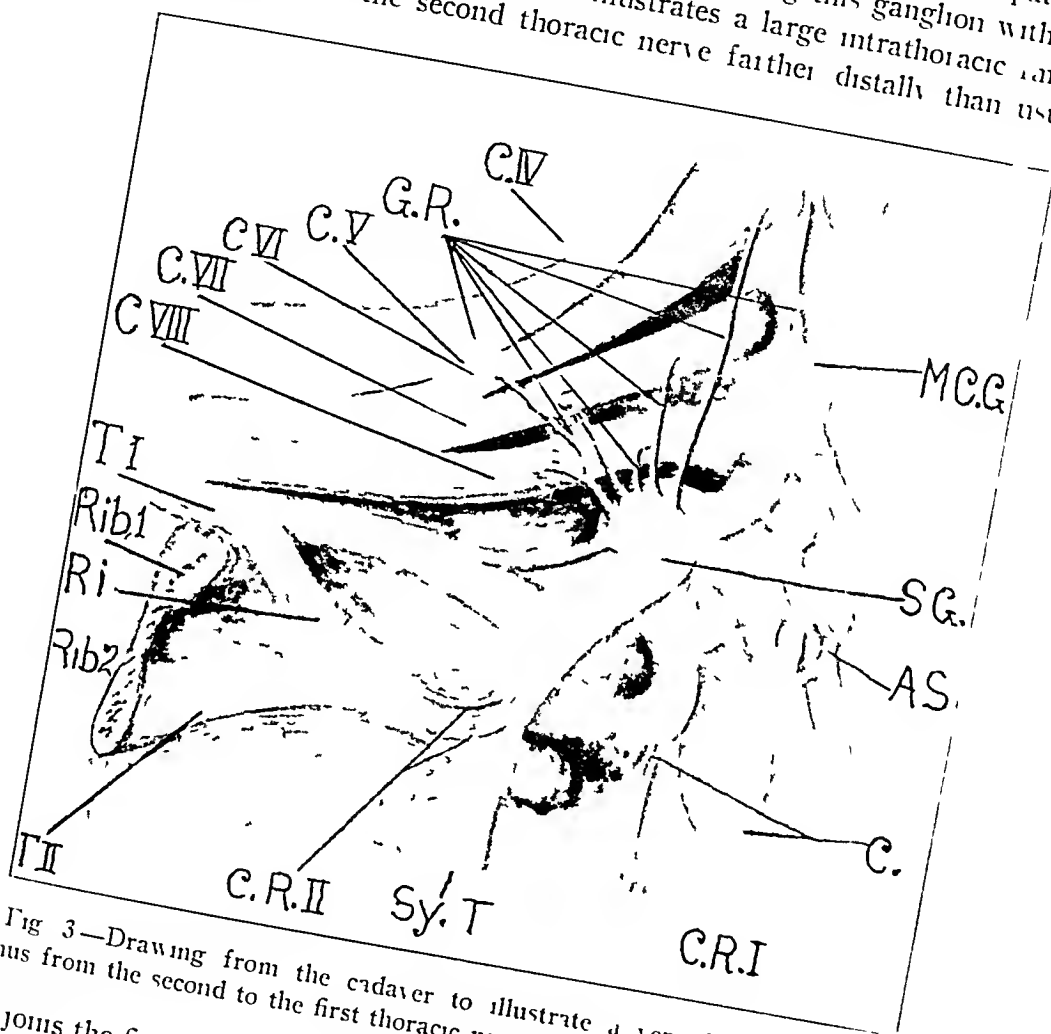


Fig 3—Drawing from the cadaver to illustrate a very large intrathoracic ramus from the second to the first thoracic nerve

but joins the first thoracic nerve proximal to the origin of its intercostal ramus. Microscopic study of sections of the intrathoracic ramus joining the first and second thoracic nerves taken at autopsy in two cases in which this ramus was well developed revealed that myelinated fibers occur there more frequently than they do in sections of spinal nerves distal to the communicating ramus. Fibers of small caliber with thin myelin sheaths occur in abundance in these sections. Thinly myelinated fibers

of small caliber also occur in abundance in sections of the gray ramus in these cases. These observations regarding the frequency of unmyelinated fibers in the ramus joining the first and second thoracic nerves in man were corroborated in sections of this ramus taken from animals (cats and dogs). While a small caliber and a thin myelin sheath or complete absence of myelin are not absolute criteria of the sympathetic nature of nerve fibers, the majority of these fibers in the ramus doubtless are sympathetic.

The foregoing observations show clearly that the intrathoracic ramus connecting the first and second thoracic nerves, which is present in man in a large percentage of cases, contains sympathetic fibers. Whenever this ramus joins the first thoracic nerve proximal to the origin of the first intercostal nerve it constitutes a pathway through which sympathetic fibers that leave the sympathetic trunk below the stellate ganglion enter the brachial plexus.

Recent studies of the innervation of the arteries of the extremities in mammals (Hirsch, 1925,² Wiedopf, 1925,³ and Kerper, 1927)⁴ show clearly that sympathetic fibers which are carried peripherally in the larger nerve trunks join the arteries at intervals along their course. Sympathetic fibers reach the vessels of the extremities mainly via these nerves. Few if any sympathetic fibers extend peripherally along the walls of the vessels. The nerves that supply the voluntary muscles include not only the sympathetic fibers which, as shown by Boeke (1913, 1927)⁵ and others, terminate on striated muscles, but also sympathetic fibers which supply the blood vessels in the muscle (Kuntz 1927)⁶. As the first thoracic nerve contributes largely to both the median and ulnar nerves, the sympathetic fibers contained in it, including those which enter via the ramus from the second thoracic nerve whenever this ramus is present, are relatively widely distributed to blood vessels and other tissues in the upper extremity.

2 Hirsch, L. Ueber die Nervenversorgung der Gefasse im Hinblick auf die Probleme der periarteriellen Sympathektomie, *Arch f klin Chir* **137** 281, 1925.

3 Wiedopf, O. Der Verlauf der Gefassnerven in den Extremitaten und deren Wirkung bei der periarteriellen Sympathektomie, *Munchen med Wchnschr* **72** 413, 1925.

4 Kerper, A. H. The Innervation of the Arteries of the Extremities, Thesis, to be published.

5 Boeke, J. Die doppelte (motorische und sympathische) efferente Innervation der quergestreiften Muskelfasern, *Anat Anz* **44** 343, 1913. Die morphologische Grundlage der sympathischen Innervation der quergestreiften Muskelfasern, *Ztschr f mikr-anat Forsch* **8** 561, 1913.

6 Kuntz, A. On the Occurrence of Sympathetic Nerve Fibers in Muscles of the Extremities Following Experimental Degeneration of the Spinal Nerves, *J Comp Neurol*, 1927, vol 43.

In view of the foregoing anatomic data extirpation of the stellate ganglion or section of the gray rami connecting this ganglion with the brachial plexus is inadequate to insure complete sympathetic denervation of the blood vessels of the upper extremity in cases in which the inconstant intrathoracic ramus connecting the first and second thoracic nerves is present. In such cases, complete sympathetic denervation of the upper extremity requires extirpation of the stellate ganglion and of the upper portion of the thoracic sympathetic trunk to the level below the communicating rami of the second thoracic nerve or section of the communicating rami of the second thoracic nerve and any peripheral rami arising from the thoracic sympathetic trunk above this level in addition to section of the gray rami connecting the stellate and middle cervical ganglions with the brachial plexus.

EXOPHTHALMIC GOITER

PATHOLOGIC CHANGE AS A RESULT OF THE ADMINISTRATION OF IODINE (LUGOL'S SOLUTION)*

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As early as 1600 B C, the Chinese used the ash of seaweed and sponges in the treatment of goiter empirically. The use of iodine in this form continued through ancient, medieval and modern times until the introduction of the pure drug in the treatment of the thyroid gland by Comdet in 1820, which followed closely the isolation of iodine from the ash of burnt sponges and seaweed by Fyfe. Comdet reported excellent results following the administration of from five to twenty drops of the tincture daily. France used iodine extensively in the Department of the Seine about 1853. It was used in the form of a powder in the food or as an ointment, which is an interesting example of the popular use of iodine at this time. Baumann discovered that iodine was a normal constituent of the thyroid gland in 1895, and this gave a more reasonable basis for its use.

Wharton, in 1656, gave the first satisfactory description of the thyroid gland and named it. A century previously, Vesalius had described the gland, and some knowledge of the external deformity and clinical symptoms of thyroid disease was prevalent among the ancients. The Romans during the time of Caesar believed that a large neck was characteristic of the Gauls and it was recognized that slaves with bulging eyes fatigued easily. The ancients of this period, however, failed to recognize the thyroid gland as different from other glands of the neck and spoke of the enlargement as bronchocels.

Parry, in 1786, first described exophthalmic goiter, it was described by Graves in 1836 and by Basedow in 1840. This was the most important advance in clinical differentiation until the present time, and ranks with Baumann's discovery of the presence of iodine in the thyroid gland as a necessary step in the later rational use of iodine in the treatment of goiter.

The mortality rate attending thyroidectomy was at first high, but was later greatly reduced through the efforts of Theodor Kocher, C H Mayo, Halsted, Crile, Ochsner, H S Plummer and others.

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Plummer,¹ in 1913, published important data on the clinical and pathologic relationship of exophthalmic goiter. He differentiated exophthalmic goiter and hyperfunctioning adenomatous goiter and thus established the clinical foundation for the advantageous use of iodine.

Kendall² isolated thyroxin as a pure chemical compound in 1914. Plummer, in 1922, introduced iodine in the form of Lugol's solution in the preoperative and postoperative treatment of patients with exophthalmic goiter, starting its use at a time when iodine for this purpose was considered inadvisable and dangerous. By differentiating adenomatous goiter with hyperthyroidism and exophthalmic goiter, Plummer had made it possible to avoid the danger of indiscriminate use of iodine and its subsequent bad results in cases of adenomatous goiter. The lack of this differentiation had been a stumbling block in the progress of treatment by iodine and had been partially responsible for its unpopularity. The use of iodine in the treatment of exophthalmic goiter was the result of observations begun by Plummer in 1913. In an article published in 1925 he says, "While preparing an article for publication in *Oxford Medicine*, I suddenly became convinced that there are many reasons why the action of iodine might have been misinterpreted. The chief of these was the lack on the part of observers of a correlation of the fluctuating findings throughout the course of the disease on a clear-cut hypothesis of the presence of two factors whether or not the factors are two products of the thyroid gland."³

The theory on which Plummer first used iodine was based on the assumption of two thyroid secretions in cases of exophthalmic goiter: the first a normal secretion, the second an abnormal one, the normal secretion causing the symptoms of hyperthyroidism, the abnormal causing the characteristic toxic symptoms and the ratio between the two secretions varying at different times in the course of the disease being influenced by the amount of iodine present, the degree of stimulation, the training and fatigue of the thyroid gland and probably unknown factors. With regard to the training of the gland Plummer writes: "The hypothesis that periods of intensive stimulation alternating with periods of remissions, provided exacerbations and remissions happened to be favorably timed, will cause a physiologic as well as an anatomic hypertrophy of the thyroid has, like most of the hypotheses presented in

1 Plummer, H. S. The Clinical and Pathological Relationship of Simple and Exophthalmic Goiter, *Am J M Sc* **146** 790-795, 1913.

2 Kendall, E. C. The Isolation in Crystalline Form of the Compound Containing Iodin which Occurs in the Thyroid. Its Clinical Nature and Physiological Activity, *Tr A Am Phys* **30** 420-449, 1915.

3 Plummer, H. S. The Function of the Thyroid Gland. Collected Papers of The Mayo Clinic and The Mayo Foundation **17** 473-499, 1925.

this paper, been daily checked against the findings of the disease in the analysis of cases under observation" ⁴

Plummer writes with regard to iodine "Many reactions that might follow the administration of iodine were considered. The complete iodination of the thyroxin molecule in the tissues of the body seemed possible but not probable. That the iodine might lead to more complete iodination of thyroxin in the gland or that it might block its discharge seemed more probable. Irrespective of the degree of stimulation the thyroid will not elaborate much of the abnormal secretion if a sufficient amount of the iodine is available" ⁵

The pathology of exophthalmic goiter has been well described by MacCallum, ⁶ Wilson, ⁶ Hamig ⁷ and others who supported the view that there are constant pathologic features and by Vichow, Kochei and others who opposed this view.

Marine's ⁸ work on the relationship of iodine to the prevention of hyperplastic changes in the thyroids of dogs, following resection of part of the gland and the relationship of iodine to the hyperplasia of exophthalmic goiter, that of Halsted, Victor Horsley ⁹ and others on the hypertrophy of the thyroid following the removal of part of the gland, with Halsted's ¹⁰ observation that if the gland of a female dog is removed before pregnancy the pups at birth will have enlarged thyroids, the work of Giordano and Caylor, ¹¹ who in studying the thyroids removed after ligation of the superior thyroid artery found that there

4 Plummer, H. S. *Functions of the Normal and Abnormal Thyroid Gland*, Oxford Medicine, New York, Oxford University Press, 1921, vol. 3, pp. 839-873.

5 MacCallum, W. G. *The Pathology of Exophthalmic Goiter*, J. A. M. A. **49** 1158-1162 (Oct. 5) 1907.

6 Wilson, L. B. *The Relationship of the Clinical and Pathologic Aspects of Exophthalmic Goiter*, Northwest Med. **5** 1-5, 1913, *The Pathology of the Thyroid Gland in Exophthalmic Goiter*, Am. J. M. Sc. **146** 781-790, 1913, *Notes on the Pathology of Simple and Exophthalmic Goiter*, M. Rec. **84** 373-378, 1913, *A Study of the Pathology of the Thyroids from Cases of Toxic-Non-Exophthalmic Goiter*, Journal-Lancet **34** 93-97, 1914.

7 Hamig, Gottfried. *Anatomische Untersuchungen uber Morbus Basedowii*, Arch. f. klin. Chir. **55** 1-68, 1897.

8 Marine, David. *On the Occurrence and Physiological Nature of Glandular Hyperplasia of the Thyroid (Dog and Sheep) Together with Remarks on Important Clinical Human Problems*, Bull. Johns Hopkins Hosp. **18** 359-364, 1907.

9 Horsley, Victor. *The Pathology of the Thyroid Gland*, Brown Lectures, Lancet **2** 1163-1164, 1886.

10 Halsted, W. S. *An Experimental Study of the Thyroid Gland of Dogs with Special Consideration of Hypertrophy of this Gland*, Rep. Johns Hopkins Hosp. **1** 373-422, 1896.

11 Giordano, A. S., and Caylor, H. D. *Histological Study of the Effect of Ligation of the Thyroid Vessels in Exophthalmic Goiter*, Surg. Gynec. Obst. **36** 75-80, 1923.

are changes at the superior pole of the gland similar to those described by Marine in the hyperplastic glands of dogs and sheep following the administration of iodine, and the excellent results obtained by Plummer¹² following the administration of iodine preoperatively to patients with exophthalmic goiter (thus lowering the surgical mortality from 35 to 1 per cent, and causing the almost complete cessation of preoperative ligations) led to the present study to determine whether these thyroids were showing histologic changes as a result of this treatment.

The thyroid gland which has undergone the characteristic exophthalmic changes is slightly larger, and there is an increase in the vascularity and an increase in the stroma especially late in the sequence, as pointed out by Marine. There is an increase in the number of the cells lining the acini which varies greatly in different glands and often in the same gland, and a change in type from cuboidal to columnar in the epithelial cells lining the acini. There is an infolding which produces hillock-like elevations into the acini or sharp projections. The colloid is less than in the normal gland and may be almost absent. In the lumen of various acini spriglike processes, as described by MacCallum and Wilson, are found. Scattered throughout the gland are numerous lymphocytic cells which may be arranged in the form of a lymphoid nodule or be present in areas without apparent arrangement. Macroscopically the superficial blood vessels appear larger than in the normal gland. The cut surface appears "meaty" with a fine lobulation.

Previous to this study, Broders had noted a change in the thyroid glands which were brought to his laboratory for diagnosis following the administration of Lugol's solution. The frozen section showed less columnar epithelium and hyperplasia, and there was more difficulty in making a diagnosis. At this time also, clinical results pointed to a change in the gland. Plummer noted "The disappearance of the characteristic nervous phenomena including the crisis death, cessation in the development of exophthalmos and in some cases rapid regression with a reduction of the entire physiologic status to that of hyperfunctioning adenomatous goiter except for the anatomic findings in the thyroid the exophthalmos and minor physical findings which remain an index of the preexisting status unless the patient is too near a moribund state before iodine is started."²

With the disappearance of the toxic symptoms the basal metabolic rate began to drop. This led Plummer to conclude that the abnormal product had a catalytic action. Cases, however, in which the symptoms were due apparently to an excess of thyroxin alone showed little change in the clinical picture or metabolic rate. Plummer said "No drop or

12 Plummer H. S. and Boothby W. M. The Value of Iodine in Exophthalmic Goiter. *I. Iowa M. Soc.* 14: 66-73 1924.

basal metabolism is obtained in those cases with high basal metabolic rates and in which the clinical picture is entirely attributable to an excess of thyroxin in the body, however, there is some evidence that iodine temporarily to a degree checks delivery of thyroxin'³

This remarkable change in the patient was accompanied by a palpable change in the thyroid gland on physical examination. The change in the clinical picture, falling metabolic rate, relief of toxic symptoms, improvement in the general condition and palpable change in the gland suggested an anatomic condition less active than that before the administration of the iodine. The cases in which the basal metabolic rate did not fall, showing little change clinically, were not investigated separately. It is probable, however, judging from this study, that active hyperplasia and hypertrophy of the gland remain.

It was realized, as pointed out by Wilson,¹³ that the only way in which the problem could be approached without laying oneself open to erroneous conclusions due to changes in the gland brought about by remissions, erroneous clinical diagnoses, previous iodization in the supposedly noniodinized cases, the possibility that individual thyroids do not absorb iodine in like amounts with similar results and other unknown causes was by a comparative study of the glands in a large number of cases, in some of which iodine had been given. Hyperplastic glands were chosen in cases in which exophthalmic goiter had been diagnosed previous to operation and which were free from adenomas large enough to cause recognizable deformity macroscopically, and relatively free from small adenomas only detectable microscopically. This selection of glands reduces the percentage error from wrong diagnoses to a fraction of 1 per cent, according to Plummet.

The method followed in this series was to study the epithelium of the acini, the connective tissue, blood vessels and lymphocytic cells of the stroma and the colloid found in the acini, and to compare and contrast the results (with and without the administration of iodine). Paraffin sections of 200 thyroids were studied, 100 of the patients had received Lugol's solution and 100 had not. Only those glands which showed pathologic changes characteristic of exophthalmic goiter as mentioned were selected. The pathologic changes were graded on a basis of 1 to 4. All the thyroids were, in this manner, divided into four groups, 1, 2, 3 and 4. The grade represents a quantitative estimate of the extent of pathologic change as shown in the table. As an example, in a case in which iodine had been given colloid was graded 4, meaning that the gland belonged to the group containing the most colloid, hyperplasia was graded 1, columnar epithelium was graded 1 and the number

13 Wilson, L. B. Personal communication to the author

of lymphocytes was graded 1, meaning that in these three histologic details the gland belonged to the group showing the least pathologic change of all the four groups. The figures are plotted in curves to show the results graphically (figs 1, 2 and 3).

The results of animal experimentation are discussed in the consideration of the results obtained by a study of this series of cases but it should be held clearly in mind that the only relationship is an anatomic similarity, and the fact that in both cases iodine had been given. The fact that iodine in both cases is associated with similar anatomic changes gives a false impression of an identity of physiologic processes for which there is so far no proof. The animal experimentation has been carried out under conditions which produced iodine deficiency or glandular deficiency, while the physiology of exophthalmic goiter is much more complicated and deals with many physiologic processes, yet

Effect of Administration of Iodine on Grading of Amount of Colloid and Degree of Hypertrophy and Hyperplasia in Thyroid Glands

Grade	Iodine Administered			No Iodine Administered		
	Colloid (Thyroid)	Hypertrophy (Thyroid)	Hyperplasia (Thyroid)	Colloid (Thyroid)	Hypertrophy (Thyroid)	Hyperplasia (Thyroid)
4	76			12	14	48
3	22	14	11	14	36	18
2	2	18	31	26	28	18
1		55	52	48	22	10

* Lymphocytic tissue is much the same in both groups. There is too little increase in this series to justify a statement.

unknown, as etiologic factors. Giordano's and Caylor's work on ligated thyroids is also discussed. Here again the inclusion has only an anatomic basis, except for the clinical fact that preoperative ligation is rarely necessary since the introduction of iodine.

CHANGE IN AMOUNT OF COLLOID

The most noticeable change in the thyroids after the administration of iodine is the increase in the amount of colloid. A typical thyroid in exophthalmic goiter, as has long been recognized, has little colloid. The amount of colloid may be so increased as to give a histologic picture similar to that of colloid goiter in which there are hyperplastic areas. The colloid in these thyroids also stains lighter and does not present the vacuolated appearance that is found in cases of exophthalmic goiter in which iodine has not been given (figs 4 and 5). The cut surface of these glands is similar to colloid glands macroscopically. The follicles are filled with clear viscid colloid which makes the gland appear translucent and a lighter red.

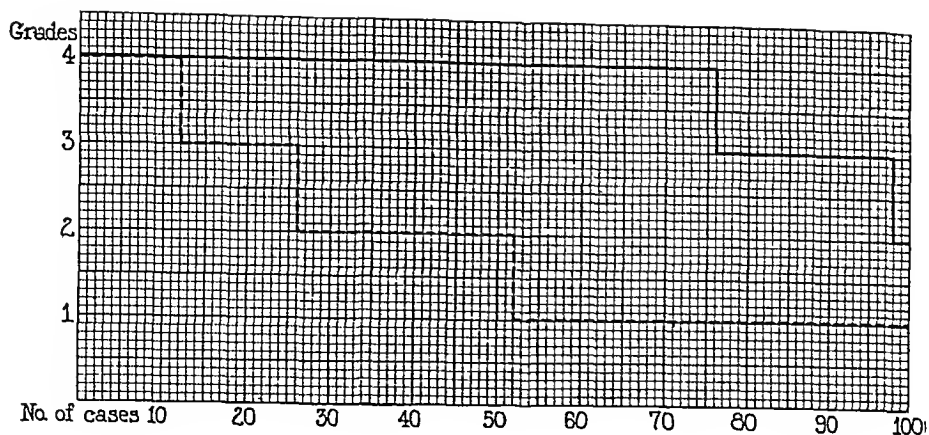


Fig 1—Comparative amounts of colloid in the thyroid glands in cases of exophthalmic goiter in which iodine was and was not administered, in this and the following figures the solid line represents the number of glands and grading when iodine was given, and the broken line when it was not given

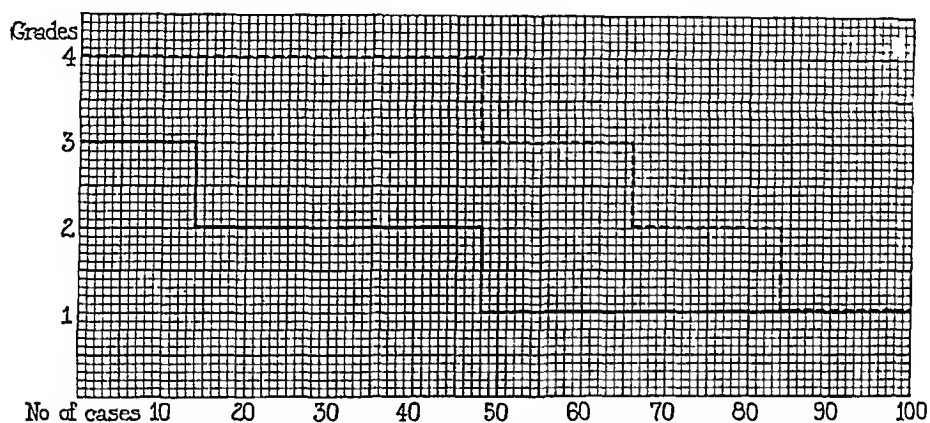


Fig 2—Comparative degrees of hyperplasia of the thyroid gland in cases of exophthalmic goiter in which iodine was and was not administered

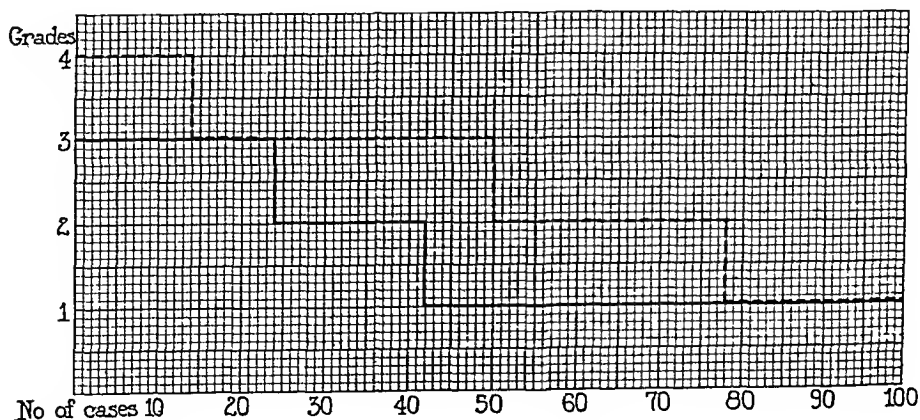


Fig 3—Comparison of the amount and extent of columnar epithelium in the thyroid gland in cases of exophthalmic goiter in which iodine was and was not administered

Marine and Williams¹⁴ in 1908 published the results of a study of seventeen patients with exophthalmic goiter who had been treated with iodine preoperatively and came to the conclusion that there was an increase in the colloid following iodization. The study on glands from

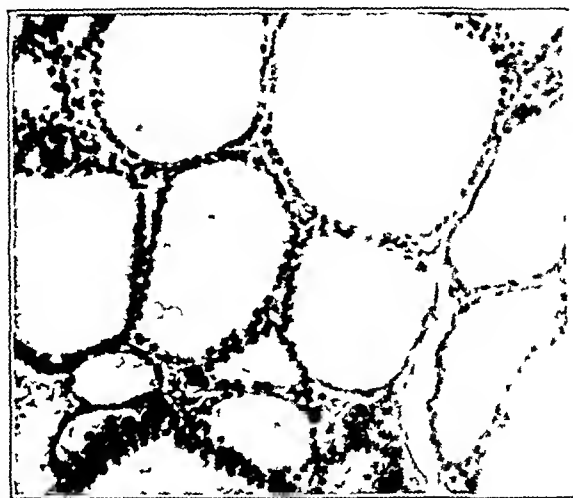


Fig 4—A thyroid gland (after the administration of iodine) in which colloid was graded 4, hypertrophy graded 1 and hyperplasia graded 1 ($\times 120$)

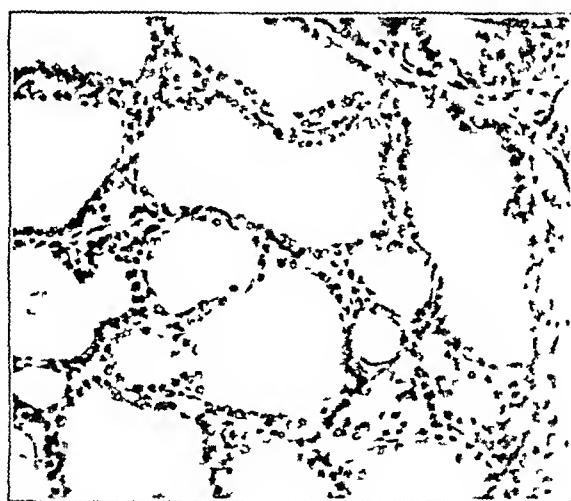


Fig 5—A thyroid gland (after the administration of iodine) in which colloid was graded 3 and hyperplasia and hypertrophy each graded 2 ($\times 120$)

patients was a small part of the work reported which discussed fully the effect of iodine on the hyperplastic glands of dogs. Thyroid glands from dogs, sheep and other animals were studied. Hyperplasia was brought about by a removal of part of the gland. The present observations

¹⁴ Marine, David, and Williams, W. W.: The Relation of Iodine to the Structure of the Thyroid Gland. *Arch. Int. Med.* 1: 349-384 (May) 1908.

hyperplasia and hypertrophy was recognized by Wagener¹⁵ in 1884 and described clearly by Victor Horsley in 1896¹⁶ Welch¹⁷ in 1888 also mentioned the phenomenon and described Halsted's work on the subject Halsted¹⁸ mentioned in addition, the part played by iodine in the prevention of hyperplasia Horsley had previously found (1886) that, following partial removal of the thyroid gland from dogs hyperplasia and hypertrophy occurred with engorgement of the blood vessels and diminution of colloid In one case the dog was killed 160 days after operation The animal a young female had exercised the function of a parent and increased in weight and size during this period Horsley¹⁶ said 'The lobe of the gland that was left became hypertrophied so as to be four to five times its normal size Increase in the activity of the organ appeared therefore to cause a decrease in the consistence of the colloid and this was contrasted with the greater solidification of the acinar contents that occurred when the function of the gland was less active'

Oswald,¹⁹ in 1902, called attention to the fact that the iodine content of goiters varies directly with the amount of colloid present This was a step in advance, as Baumann who had discovered the presence of iodine had drawn the erroneous conclusion that there was always less iodine in goiters than in normal thyroid glands which Oswald points out, was a result of his dealing with glands that contained little colloid Marine and more recently, Cattell²⁰ concluded that the amount of colloid and iodine varied proportionately

I found that in seventy-six of the total 100 glands studied, there were more marked changes (graded 4) in the colloid after the administration of iodine In these the colloid was evenly distributed and distended practically all acini of different parts of a section Twenty-two of the glands were graded 3, they showed slightly less colloid there

15 Wagener Ueber die Folgen der Exstirpation der Schilddrüse nach Versuchen an Thieren Wien med Bl 1884 nos 25 and 30

16 Horsley, Victor A Discussion on the Pathology of Exophthalmic Goiter, Brit M J 2 895, 1896

17 Welch, W H Demonstrations of Pathological Anatomy Microscopical Specimens of the Thyroid Gland After Partial Extirpation M News 3 455, 1888

18 Halsted W S Factors Which May Be Concerned in Causing Hypertrophy of the Thyroid Gland and the Effect of Excision of this Organ upon Other of the Ductless Glands, Tr A Am Phys 28 127-135 1913

19 Oswald A Die Chemie und Physiologie des Kropfes Virchow's Arch 1 path Anat 169 444-479 1902

20 Cattell R B The Pathology of Exophthalmic Goiter A Histological and Chemical Study of the Change Following Administration of Iodine (Lugol's Solution) Boston M & S J 192 989-996 1925

being areas in which the acini were full of colloid but also small areas in which it was almost absent. Colloid in the other two glands of the group was graded 2. In the 100 other glands (no iodine having been given) twelve were graded 4 as to colloid, fourteen were graded 3, twenty-six were graded 2 and forty-eight were graded 1.

In the cases in which iodine was given and in those in which it was not given, the amount of colloid increased as the amount of hyperplasia decreased, a point mentioned in 1908 by Marine and Williams as true in general for thyroid glands. As a check on the accuracy of the grading, the average grade of hyperplasia in each of the four grades of colloid was estimated in both types of gland. This also gives clearly the idea of the inverse ratio between the amount of colloid and the extent of hyperplasia. In the thirteen glands (without the administration of iodine) graded 4 for colloid, the average grade of hyperplasia was 1.53, in the fourteen glands graded 3, the average grade of hyperplasia was 1.55, in the twenty-six glands graded 2, the average grade of hyperplasia was 3.7, and in the forty-eight in which colloid was graded 1 the average grade of hyperplasia was 3.76. After the administration of iodine seventy-six of the glands were graded 4 for colloid with an average grade of hyperplasia of 1.6, twenty-two were graded 3 with an average grade of hyperplasia of 1.9 and twenty were graded 2 with an average of grade 3 for hyperplasia.

Attention should be directed to the work of Giordano and Caylor with regard to the effect of ligation of the superior pole of the thyroid gland on the histologic appearance of the gland, before iodine was used and in the preoperative preparation of patients for partial lobectomy. "The most constant finding of the early period in the sections taken near the ligated areas was a tendency for the lumina of the follicles to be large and filled with colloid." Summarizing, it may be concluded that as the thyroid is iodinated the amount of colloid increases and the hyperplasia and hypertrophy decrease. A review of some of the experimental work in animals shows an interesting relationship between hyperplasia, colloid and iodine deficiency in this group. The investigations of Marine and Giordano and Caylor on the glands of human beings show the same anatomic picture with regard to colloid that I have noted.

CHANGE IN DEGREE OF HYPERPLASIA

The word hyperplasia is used here to describe a condition in the parenchyma of the gland in which the number of cells appeared to increase, although this was not proved. The hyperplasia noticeably decreases after the administration of iodine, which coincides with the relationship of colloid and hyperplasia (figs 6 and 7). With the dis-

cussion of hyperplasia the question of mitosis arises, but since I noted the condition so infrequently it is not of significance here

In forty-eight glands (without iodine) graded 4 hyperplasia was graded 3 in eighteen, in eighteen it was graded 2 and in sixteen it was graded 1. In fourteen glands, after the administration of iodine, hyper-



Fig 6—A thyroid gland in which colloid was graded 2 and hyperplasia and hypertrophy each graded 3 (no iodine was administered), $\times 120$

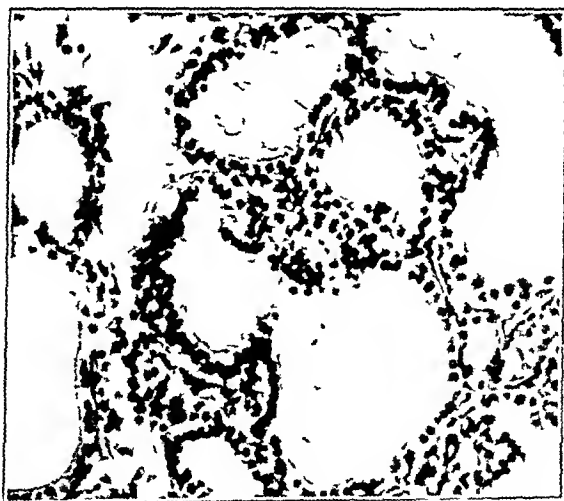


Fig 7—A thyroid gland (after the administration of iodine) in which colloid was graded 2 and hyperplasia and hypertrophy each graded 3, $\times 120$

plasia was graded 3, in thirty-four it was graded 2 and in fifty-two it was graded 1. As will be shown when the grades for the various degrees of hypertrophy are given later, there is a direct relationship between hyperplasia and hypertrophy, while that between colloid and hyperplasia is indirect.

Marine, in writing on the pathologic anatomy of exophthalmic goiter, stated that as the colloid accumulates in the gland during a regressive stage, the high columnar epithelium with its infoldings slowly returns to cuboidal. If the involution to a colloid type of gland is complete, the infoldings take on more of the appearance of small tufts of stroma jutting into the follicular lumen covered with the prevailing type of epithelium. Marine and Lenhart,²¹ discussing the reversion taking place in the thyroid in cases of exophthalmic goiter not treated by iodine, described anatomic changes that cannot be differentiated from the change which takes place in the gland in exophthalmic goiter after treatment with iodine, except that after treatment with iodine there seems to be more of a tendency for the hyperplasia to disappear without leaving a trace of its presence in the form of the tufts already described.

Halsted, in 1896, predicted the foregoing anatomic changes in the goiters after iodine had been given, although he was discussing the anatomic changes which would take place during reversion of an exophthalmic gland to a normal anatomic state. "Change backward from hypertrophy to normal would be a simple matter, the shrinkage of the epithelium, the atrophy of the new if indeed they are new blood vessels and the formation of normal colloid, would accomplish the transition."

The experimental production of hyperplasia and hypertrophy by Horsley, Marine, Loeb and others²² in the thyroid glands of dogs, guinea-pigs, monkeys, sheep and goats was uniformly successful. All agreed, with the exception of Loeb, that the administration of iodine would either prevent hyperplasia in these glands or cause it to decrease or disappear. Loeb found that the administration of iodine in guinea-pigs had no effect on the hyperplasia of the gland and concluded that there was a slight increase in the hypertrophy and hyperplasia in his animals after they had received iodine. Giordano and Caylor observed

21 Marine, David, and Lenhart, C. H. The Colloid Glands (Goitres), Their Etiology and Physiological Significance, *Bull. Johns Hopkins Hosp.* **20** 131-139, 1909, The Pathological Anatomy of the Human Thyroid Gland *Arch. Int. Med.* **7** 506-535 (April) 1911, Pathological Anatomy of Exophthalmic Goiter, *ibid.* **8** 265-316 (Sept.) 1911.

22 Loeb, Leo. Studies on Compensatory Hypertrophy of Thyroid Gland. IV The Influence of Iodine on Hypertrophy of the Thyroid Gland, *J. M. Research* **41** 481-494, 1919-1920, Studies on Compensatory Hypertrophy of the Thyroid Gland. V The Effect of the Administration of Thyroid, Thymus Gland and Tethelin and of a Meat Diet on the Hypertrophy of the Thyroid Gland in Guinea-Pigs, *ibid.* **42** 77-89, 1921. Loeb, Leo and Kaplan, E. E. Studies of Compensatory Hypertrophy of the Thyroid Gland. VI The Effect of Feeding Anterior Lobe of the Pituitary Gland on the Hypertrophy of the Thyroid Gland in the Guinea-pig, *J. M. Research* **44** 557-578, 1924.

in the glands removed following preoperative ligation an increase in the number of spriglike processes, which MacCallum has considered the remains of hyperplastic tufts, with a decrease of the amount of actual hyperplasia.

Marine suggested that the reason for the infolding that accompanies hyperplasia is mechanical, dependent on the increase in the number of cells, without a corresponding increase in the acinus. Marine and Lenhart, in 1911, called attention to the fact that these infoldings are less marked in nonencapsulated glands, as in fish.

The change taking place in the gland in exophthalmic goiter after iodine has been given is similar to that described by Marine during reversion in exophthalmic goiter and similar to what Halsted predicted would occur during reversion of a hyperplastic gland to normal. A



Fig 8—A thyroid gland in which colloid was graded 1 and hypertrophy and hyperplasia were each graded 4 (no iodine was administered), $\times 120$

review of some of the experimental work shows a close relationship between hypertrophy, hyperplasia, colloid formation and the ingestion of iodine and the anatomic pictures, after the administration of iodine, are similar to those observed in this study. Again, in reviewing the work of Giordano and Caylor, a similar anatomic picture is noted. It is probable that, in the case of the ligated thyroid, much the same condition is produced as by removal of thyroid tissue, while the administration of iodine brings about a condition of the gland which is more nearly normal physiologically and anatomically.

CHANGE IN DEGREE OF HYPERTROPHY

I have considered that the extent and nature of the columnar epithelium provided an index of the degree of hypertrophy. The columnar epithelium also changed after the administration of iodine. It was not present in as large quantity. There was a marked increase in the amount

of cuboidal epithelium lining the acini (figs 8 and 9), a certain variable percentage of which was low cuboidal and some so flat as to lose even the characteristics of low cuboidal epithelium, the cells being low in proportion to their width at the base. In the cases in which iodine was given, the extent of columnar epithelium was never graded 4, whereas of the other 100 it was graded 4 in fourteen it was graded 3 in twenty-four and thirty-six respectively, graded 2 in eighteen and twenty-eight respectively and graded 1 in fifty-eight and twenty-two respectively.

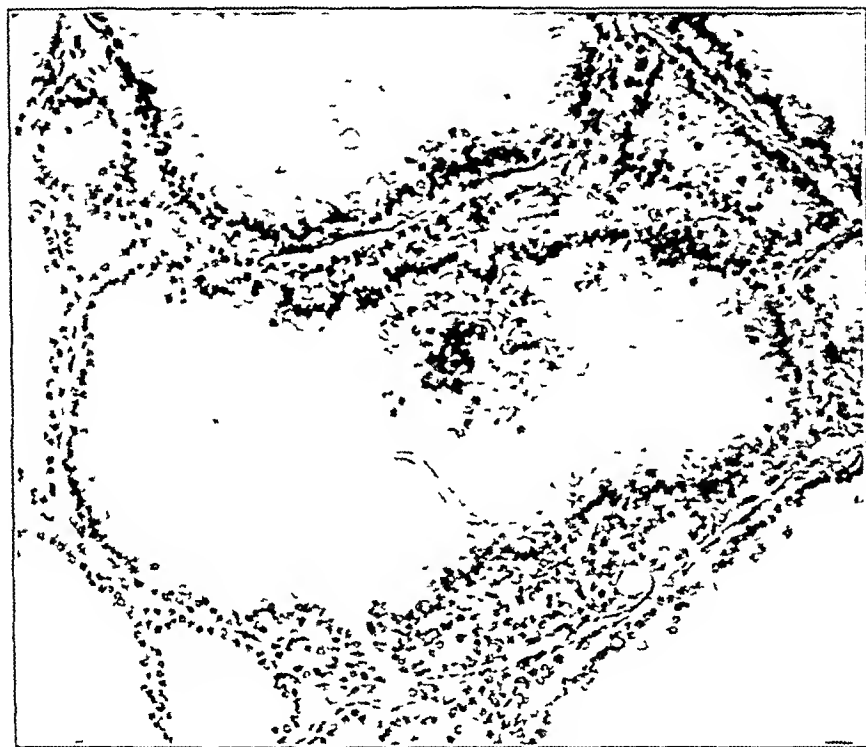


Fig 9—A thyroid gland (after the administration of iodine) showing active hyperplasia and also a large amount of colloid suggesting that the appearance of colloid is the first change following iodimization, $\times 120$

The decrease observed in the amount of hypertrophy agrees with the conclusions of Marine and Williams in 1908 and of Cattell and Rienhoff²³ in recent papers which will be reviewed later.

It is interesting to note that in this histologic detail the results are similar to those obtained by Giordano and Caylor, in the work already quoted. Marine found a decrease in the hypertrophy combined with the hyperplasia in the experimentally produced hyperplasia of the thyroid of dogs.

²³ Rienhoff, W. F. The Historical Changes Brought About in Cases of Exophthalmic Goiter by the Administration of Iodine, *Bull. Johns Hopkins Hosp.* 37: 285-306, 1925.

CHANGES IN THE STROMA

Under the heading of changes in the stroma I shall consider blood vessels, connective tissue and lymphocytic cells

Marine, MacCallum and Wilson pointed out the increase in the amount of connective tissue in the thyroid in cases of exophthalmic goiter. It is easily recognized, and all observers agree regarding its presence

In the present study there appeared to be less connective tissue relative to the amount of parenchymatous tissue and colloid speaking quantitatively, after the administration of iodine (fig 10). Whether this indicated that there were fewer connective tissue cells was due to mechanical pressure or was simply a relative increase in the amount of



Fig 10—Typical thyroid gland after the administration of iodine colloid distending acini, little hypertrophy and hyperplasia, cells cuboidal and flat with occasional hyperplastic and hypertrophic areas sufficiently marked to justify its classification as unmistakably a hyperplastic gland, $\times 120$

colloid could not be ascertained from the sections examined. The histologic picture, however, suggested rather that it was a pressure phenomenon caused by the distention of the acini and consequent relative decrease in stroma generally. It is to be noted that the greatest amount of colloid is often locally associated with the least amount of columnar epithelium, and between such acini there is often little stroma. This suggests the operation of a mechanical factor to make the stroma appear less.

The lymphocytic areas present in the gland after the administration of iodine presented the same anatomic picture as when iodine was not given. They were present in small nodes or without organization. Apparently there was not any increase or decrease.

The blood vessels seemed smaller by comparison although I could not be sure of this as the change if any, was so small as to require in the larger arteries exact comparison of the same blood vessel before and after the administration of iodine. Such comparison was impossible in this study and would probably have been misleading even if practicable because of possible change in the gland not due to iodine. In the capillaries, however, there is probably a decrease in caliber, which, if present would probably necessitate a smaller arterial supply or a lessened blood flow amounting physiologically to the same thing.

Giordano and Caylor observed an increase in the amount of connective tissue in the areas adjacent to the ligated superior pole, where the changes described by them occurred. In a few cases this change was so extensive as well to deserve the name given by Marine of 'cirrhosis of the thyroid gland'. It is impossible to do other than surmise the reason for the increase in the connective tissue found by Giordano and Caylor. It seems logical to believe that all the changes are the result of diminution of the blood flow lessening nutrition to the part of the gland supplied and that the increased amount of connective tissue is evidence of degeneration. In the glands, however after the administration of iodine, the whole pathologic process associated with exophthalmic goiter in the thyroid has been retarded and a type of gland produced which is probably as near the normal as the gland may become anatomically, considering the previous anatomic change, the presence of an adequate amount of iodine and the stimulation to which the gland is subjected.

Plummer described a small group of glands in 1913 which are of special interest at this point in the study. "The sequence (in exophthalmic goiter) is an intensive stimulation from some unknown source of the entire previously normal thyroid, diffuse hypertrophy, increased output of thyroxin hyperthyroidization of the organism and, when the functional integrity of the epithelium is threatened, hyperplasia. In rare instances the stimulus may be of relatively low intensity for a considerable period causing hyperthyroidism without development of hypertrophy. There is a small group of patients having near normal or colloid glands and the clinical complex of exophthalmic goiter." I have not been able to find a previous description of this group, this being the first description noted in the literature.

Since, as I have shown, iodine brings about an increase in the amount of colloid, a decrease in the hypertrophy and hyperplasia, the small group of patients mentioned by Plummer should be enlarged. In this study the increase in the colloid seemed to be the most marked change produced by iodine, change in degree of hypertrophy the next and change in degree of hyperplasia third. This suggests the possibility, from an anatomic point of view of the presence of a change in the

colloid with little or no hypertrophy in an exophthalmic condition, provided the stimulation of the thyroid is mild. This would probably be the condition at the onset of the disease for a time, the length of which there is no way of estimating. From the standpoint of pathologic diagnosis this is important, because the use of iodine should add to this group those cases in which the gland has progressed one step farther and is hypertrophic but not hyperplastic.

Recently several noteworthy papers have appeared in the literature, two of the earliest by Cattell and Rienhoff. Cattell's conclusions are that after the administration of iodine there is a decrease in vascularity, hyperplasia and hypertrophy, an increase in colloid and a decrease in the amount of connective tissue, that lymphocytic foci remain, as well as numerous scars, and that there is an increase in the iodine content of the gland. Rienhoff's conclusions are that there is an increase in the thyroid gland as a whole, a decrease in vascularity and probably in lymph flow through the gland, a large increase in the colloid deposited and contained within the thyroid, a change in the acini from lacelike ingrowths to round, even walled acini regular in size and shape and a change in the nuclei from large clear nuclei to a small irregular pyknotic type. He observed many mitotic figures before the use of iodine, and their absence after iodine had been given.

SUMMARY

There is an increase in colloid and a decrease in hypertrophy and hyperplasia in the thyroid gland after the administration of iodine. There is probably a decrease in the amount of connective tissue and in the size of the arteries and capillaries. Iodine does not have any effect on the number of lymphocytes present.

INTRATHORACIC GOITER *

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During recent years, many articles relating to pathologic lesions of the thyroid gland have appeared in the literature, but intrathoracic goiter has received scant attention. It is with the hope of contributing something to the solution of the various problems presented by this condition that I am offering this analysis of 100 cases of complete intrathoracic goiter, together with a review of the literature.

GENERAL REVIEW OF THE LITERATURE

Attention was first focused on this condition between the years 1912 and 1916, during which period an occasional article or case report was presented in the foreign literature. Since that time, articles have appeared from time to time in both American and foreign journals.

In 1914, Key¹ described two cases of intrathoracic goiter in which operation was performed by the Sauerbruch-Schoemaker technic (resection of part of the sternum). In 1917, Lahey² described the mechanism of the production of intrathoracic goiter and discussed diagnosis and treatment. In 1918, Lamson³ reported a case of bilateral intrathoracic goiter, and described the management of the case. In 1919, Leiner⁴ reported a case of true intrathoracic goiter with symptoms of thyrotoxicosis. As the goiter was small and there were no symptoms of pressure, medical treatment was instituted and relief from symptoms resulted. In 1920, Plenk⁵ described and classified substernal goiters and discussed their operative management, advising the splitting of the sternum. In 1920, Odermatt⁶ reported a case of intratracheal struma in which operation was performed.

In 1920, Lahey⁷ again discussed etiology, diagnosis and management in cases of intrathoracic goiter, considering them as of two types—

* From the Cleveland Clinic.

1 Key, E. Ein mit Erfolg operierter Fall von intrathorakaler Struma, Nord med Ark **14** 1, 1914.

2 Lahey, F. H. Intrathoracic Goiter, Boston M & S J **176** 341, 1917.

3 Lamson, O. F. Intrathoracic Goiter, Surg Gynec Obst **27** 397, 1918.

4 Leiner, J. H. Intrathoracic Goiter, New York Med J **110** 190, 1919.

5 Plenk, A. Zur Sternumspaltung bei substernaler Struma, Deutsche Ztschr f Chir **156** 378, 1920.

6 Odermatt, W. Intratracheal Strumas, Deutsche Ztschr f Chir **157** 279, 1920.

7 Lahey, F. H. Diagnosis and Management of Intrathoracic Goiter, J A M A **75** 163, 1920.

incomplete and complete. In the incomplete type the major portion of the thyroid is in the neck and is visible and in the complete type the major portion of the gland lies within the thorax no part of the goiter being visible or palpable, except that in some cases the upper pole may be barely palpable above the presternal notch. In his discussion of surgical treatment, Lahey recommended the delivery of the thyroid as a whole into the neck rather than a piecemeal delivery with consequent hemorrhage.

In 1920, Rachford⁸ presented a case of substernal goiter in which symptoms of pressure were present. Fifteen roentgen-ray treatments were given, and improvement resulted. In 1921, Brunner⁹ gave a clinical picture of intrathoracic cystic accessory struma. In the case reported by him operation was not performed but the patient died of paralysis of the heart following an attack of grip six years later, and the diagnosis of goiter was confirmed at autopsy. Brunner cited a similar case of Dittrich's.

In 1921, Lahey¹⁰ again presented a number of case reports and described the treatment employed in each. In one case, the intrathoracic goiter was associated with hyperthyroidism. He stated that adenoma is the most frequent type of intrathoracic goiter. In order to prevent rupture of the pleura and hemorrhage, he recommended the placing of a pack in the cavity after the removal of the goiter.

In 1922, Terry¹¹ described the plunging and fixed types of intrathoracic goiter, classifying the symptoms according to interference with, or pressure on, the adjacent structures. He recommended that when division of the sternum is necessary longitudinal division be employed. In 1922, Seelig¹² reported a case in which cholelithiasis, intrathoracic goiter and hyperthyroidism were present.

Hertzler¹³ and Crotti¹⁴ have also discussed the diagnosis and management in cases of intrathoracic goiter, and articles by Wolfier,¹⁵

8 Rachford, B. K. Substernal Goiter with Pressure Symptoms, *Am J M Sc* **160** 410, 1920.

9 Brunner, H. C. Intrathoracic Cystic Accessory Strumas, *Beitr z klin Chir* **122** 114, 1921.

10 Lahey, F. H. Intrathoracic Goiter (Secondary Hyperthyroidism), *S Clin N Amer* **1** 641 (June) 1921.

11 Terry, W. I. Intrathoracic Goiter, *S Clin N Amer* **2** 489 (April) 1922.

12 Seelig, M. G. Cholelithiasis and Intrathoracic Goiter, *S Clin N Amer* **2** 1549 (Dec) 1922.

13 Hertzler, A. E. Diseases of the Thyroid Gland. St. Louis, C. V. Mosby Company, 1922.

14 Crotti, A. Thyroid and Thymus, Philadelphia Lea & Febiger, 1918, p. 140.

15 Wolfier, quoted by Plenk (footnote 5).

Kocher,¹⁶ Monnier¹⁷ and Perthes¹⁸ are also of interest. In cases in which there is high stenosis Wolfler advised a primary tracheotomy, followed two weeks later by removal of the goiter. Kocher stated that exenteration may be advisable after resection of the sternum or ribs, and that, if necessary, this may be performed transpleurally. Perthes advised mediastinotomy according to the technic of Sauerbruch. Monnier reported one case in which the sternum was split and partial exenteration performed and called attention to the hemorrhage which may occur in this operation.

Molner¹⁹ recommended the preoperative use of roentgen-ray therapy to reduce the size of the intrathoracic goiter. Judd²⁰ also discussed intrathoracic goiters: classification, symptoms and treatment. He emphasized the importance of the relationship of the goiter to vital structures, the need of freeing the upper pole first and the importance of avoiding manipulation outside the fibrous capsule.

In 1923, Haberer²¹ reported a case of retrosternal struma associated with a diverticulum of the esophagus and a bleeding gastric ulcer. Strumectomy and excision of the diverticulum were performed, followed later by resection of the stomach. The ulcer was small, and the author thought that possibly healing had been prevented by the stasis in the venous circulation produced by the struma. He had frequently noticed stasis catarrh of the stomach when large strumas were present.

In 1924, in a discussion of the symptoms, diagnosis and treatment in intrathoracic goiter, Levin²² recommended the transverse division of the sternohyoid and sternothyroid muscles as providing the best exposure.

In 1924, Hunermann²³ discussed diagnosis and treatment in intrathoracic goiter and also the frequency with which this condition has been seen in his own and in other clinics. He stated that the discrepancy in incidence is doubtless due to varied methods of classification.

In 1925, Grier²⁴ discussed the use of radiation in the treatment of patients who had intrathoracic goiter, stating that amelioration of

16 Kocher, T. Text-book of Operative Surgery, London, Adam & Charles Black, 1903, p. 147.

17 Monnier, quoted by Hunermann. Arch f klin Chir **122** 789, 1923.

18 Perthes, quoted by Plenk (footnote 5).

19 Molner, A. L. A Case of Retrosternal Goiter, Klin Wchnschr **1** 420, 1922.

20 Judd, E. S. Intrathoracic Goiter, Internat Clin **1** 149, 1920.

21 Haberer. A Diverticulum of the Esophagus, a Retrosternal Goiter and a Bleeding Gastric Ulcer in the Same Patient, Arch f klin Chir **122** 789, 1923.

22 Levin, S. Intrathoracic Goiter, J Michigan M Soc **23** 208, 1924.

23 Hunermann, T. Intrathoracic Goiter, Arch f klin Chir **128** 202, 1924.

24 Grier, G. W. Is Irradiation a Satisfactory Treatment for Substernal Thyroid? Am J Rontgenol **13** 327, 1925.

the symptoms and decrease in the size of the goiter follow the use of roentgen-ray therapy in cases of adenoma and of exophthalmic goiter, while this form of treatment has no effect on colloid or cystic goiters. He concluded that if the tumor can be removed without risk, a surgical procedure is the method of choice but if considerable risk attends the operation, radiation is indicated.

In 1925, Noehren²⁵ discussed symptoms and treatment in intrathoracic goiter, and in 1926, Aleman²⁶ described two cases in which anterior mediastinotomy was performed.

CLASSIFICATION

Opinions differ greatly as to the correct grouping of intrathoracic goiters, some authors considering that only those tumors which lie entirely in the thorax should be classified as intrathoracic goiters, while others include also those in which only a portion of the goiter passes down into the thorax. A similar confusion attends the classification of substernal and subclavicular goiters. It is obvious that until a standard classification is adopted, it will be difficult to interpret correctly published reports of cases of intrathoracic goiter, as there will be discrepancies in the clinical picture, the incidence and the operative technic.

In the Cleveland Clinic, the following classification has been adopted:

I Intrathoracic Goiter

(a) Complete

The greater part (four-fifths) of the goiter lies in the thorax and only the upper pole, or none of the glands is palpable above the sternum or clavicle.

(b) Incomplete

Only a part of the goiter extends into the thorax and at least one-half is palpable in the cervical region.

II Substernal Goiter (Complete or Incomplete)

The entire goiter or a portion of it extends below the sternum.

III Subclavicular Goiter (Complete or Incomplete)

The entire gland or a portion of it extends below the clavicle.

In figures 1 to 6 are shown schematic drawings illustrating the relative positions of the two lobes of the thyroid in some of our cases of intrathoracic goiter, and roentgenograms of other cases are given in figures 6, 7 and 8.

Terry has called attention to two other types of intrathoracic goiter, the "plunging" and the "fixed" types. The "plunging" intrathoracic goiter may be raised into the neck by coughing or by violent respiratory

²⁵ Noehren A. H. Intrathoracic Goiter. *Am J Surg* 39:192, 1925.

²⁶ Aleman O. Two Cases of Anterior Mediastinotomy for Intrathoracic Struma. *Acta chir Scandinav* 60:135, 1926.

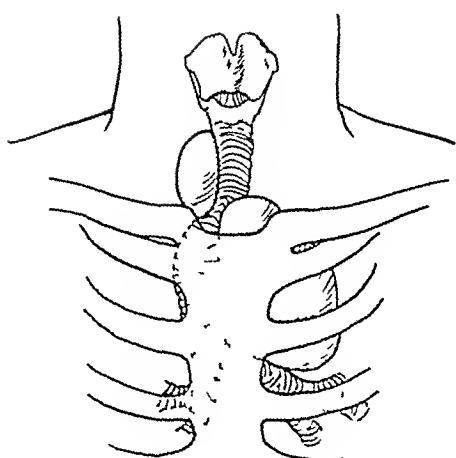


Figure 1

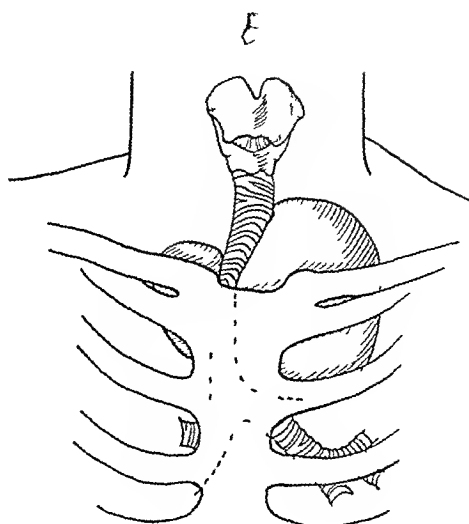


Figure 2

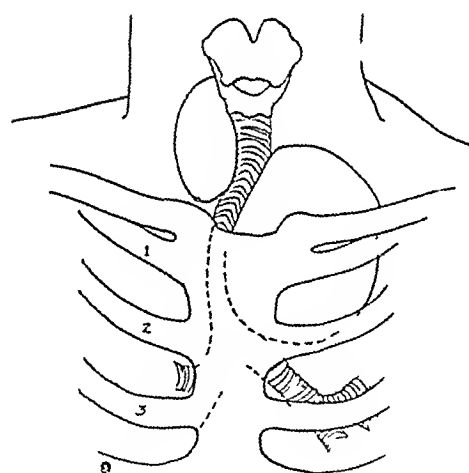


Figure 3

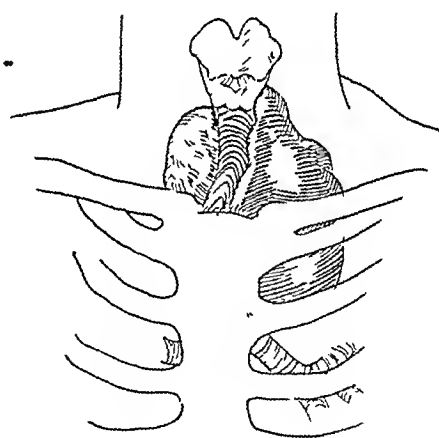


Figure 4

Fig 1—Schematic drawing showing left lobe of thyroid gland, almost entirely intrathoracic, with deviation of trachea toward the right

Fig 2—Schematic drawing showing both lobes of thyroid gland partially intrathoracic and compression of trachea

Fig 3—Schematic drawing showing right lobe of thyroid gland in normal position and large left lobe partly intrathoracic with compression and deviation of the trachea

Fig 4—Schematic drawing showing both lobes of the thyroid gland enlarged and partially intrathoracic with marked compression and deviation of the trachea

movements. Fluoroscopic examination frequently reveals a moderate extension of the goiter into the thorax, the goiter being entirely dislocated into the cervical region when the neck is extended. This is also often observed during operation. An interesting case of this type has been reported by Schworer,²⁷ on examination of his patient a complete intrathoracic goiter had been found of which only the upper portion of the left lobe was visible on swallowing. There were



Fig. 5—Schematic drawing showing the anatomic relations in a case of intrathoracic goiter.

also symptoms of hyperthyroidism. A few months after this examination the patient tossed her head backward vigorously while shampooing her hair; she felt a violent pain in her throat, became faint and had symptoms of dyspnea. The physician discovered a tumor in the anterior side of the throat between the jugular vein and the thyroid cartilage. This tumor increased in size, and when

²⁷ Schworer, B. Subkutane Strumluxation peri- und intrathoracisch. Blutung. Beitr. z. klin. Chir. **131**: 359, 1924.

the patient reached the hospital it was 12 cm in length and 6 cm in width. It was shaped like a sausage and lay in a transverse position. As palliative treatment did not relieve the condition, operation was performed the following morning. The tumor mass was found to be comprised of the left lobe of the thyroid. The lower veins of the left capsule were torn away and were drawn back toward the mediastinum in a great retrosternal hematoma. The capsule was intact, but it was tense and was blue-black. The parenchyma of the thyroid was completely destroyed and was filled with great clumps of coagulated

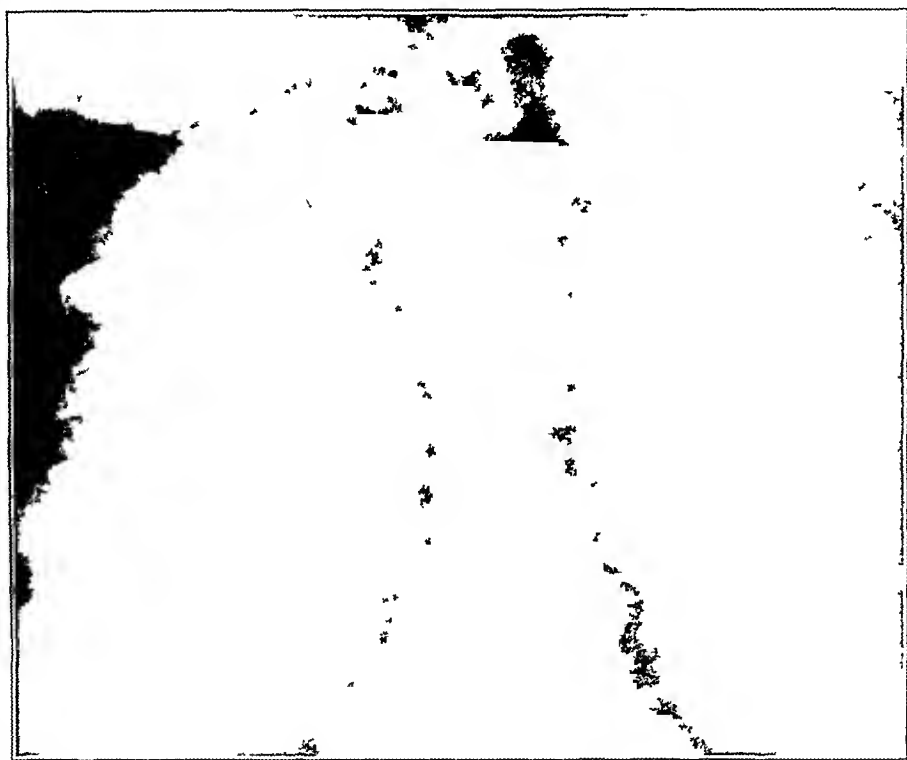


Fig 6—Roentgenogram showing the anteroposterior view of intrathoracic goiter posterior to trachea pushing the trachea forward and somewhat compressing it

blood. The patient recovered well after the operation, and the symptoms of hyperthyroidism also disappeared. The "fixed" intrathoracic goiter remains in the thorax because of adhesions or because it is larger than the aperture between the thorax and the neck.

INCIDENCE

In analyzing reports on the incidence of intrathoracic goiter, the influence of variations in methods of classification is evident.

Von Eiselsberg found a substernal projection of one or both lobes in 50 per cent of his cases, partially intrathoracic goiters in 5 per

cent and totally intrathoracic goiters without a cervical portion in 1 per cent. Crotti reported that from 25 to 35 per cent of all the goiters in his cases and in those reported by other observers lay deep in the upper thorax, while from 15 to 18 per cent were partially intrathoracic. Hertzler reported 0.25 per cent as the incidence of the latter type. Levin reported that 20 per cent of the goiters which he had seen were deep-seated, 3 per cent were deep enough to be called intrathoracic. In Leimer's series of cases of goiter, from 6 to 7 per cent were intrathoracic. According to Terry's figures, in from 7 to 10 per cent of the goiters in his series a considerable portion of the gland lay in



Fig 7—Lateral view of figure 6

the thorax. Noehren stated that in from 7 to 18 per cent of his cases the goiter was intrathoracic.

Czernak²⁸ reported that of the 1,473 cases of goiter seen in the Innsbruck Clinic from 1912 to 1920 the goiter was intrathoracic in 487 or 32 per cent. Among these cases, the left lobe was retrosternal in 251 cases, or 51 per cent, the right lobe was retrosternal in 148 cases or 41 per cent and the right and left lobes were retrosternal in 59 cases or 12 per cent. Reinbach²⁹ reported 31 cases of intra-

²⁸ Czernak, quoted by Hünemann (footnote 23)

²⁹ Reinbach, quoted by Hünemann (footnote 23)

thoracic goiter among 162 cases of goiter, an incidence of 19 per cent, Closs³⁰ reported 10 cases among 106 cases of goiter, or 9 per cent, Kocher stated that in 10 per cent of his cases the goiters were intrathoracic. Monnier found 114 cases of substernal goiter and 17 of intrathoracic goiter in a total series of 670 cases. Of the latter, the right lobe was in the thorax in 47 cases, the left lobe in 62 cases and the isthmus in 5 cases. Jackson reported an incidence of 542 substernal goiters, 13.5 per cent, and 25 intrathoracic goiters, 0.6 per cent, among 4,006 thyroidectomies performed at the Mayo Clinic for simple colloid and adenomatous goiter.

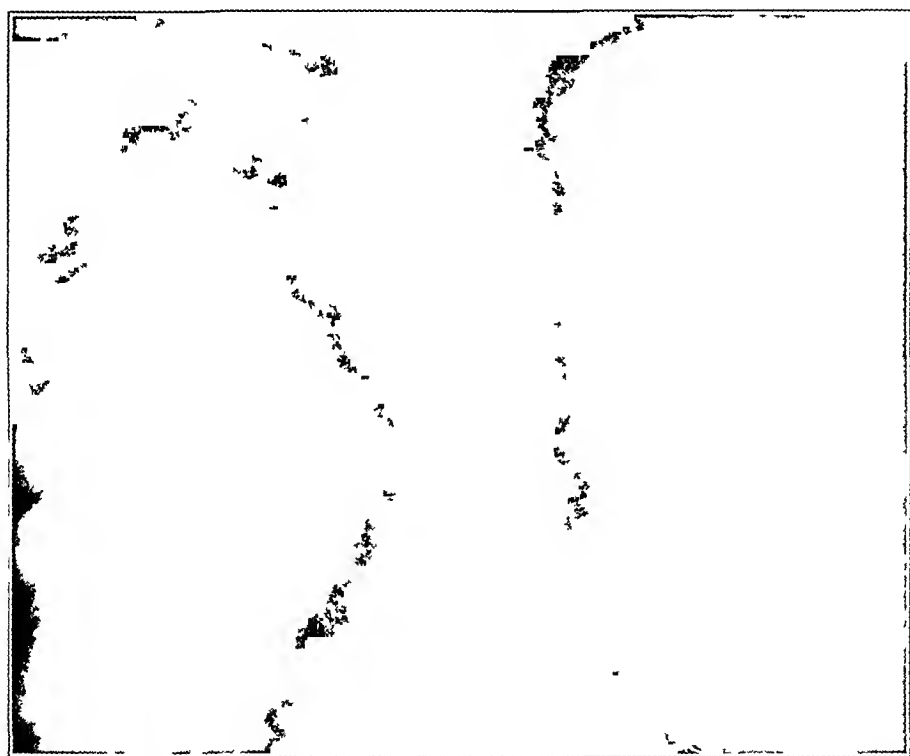


Fig 8—Roentgenogram of large intrathoracic goiter showing displacement of trachea to the right

A comparison of these figures shows a variation in the incidence of from 1 to 18 per cent. In our own series, from 1 to 2 per cent of all cases may be classified as completely intrathoracic, while approximately 10 per cent have been of the incomplete type.

Age—Intrathoracic goiter is rarely seen in children, and its incidence increases with age up to the age of 60 years. This increasing incidence is readily understood when it is realized that a goiter may occupy the cervical position for years before descending into the

³⁰ Closs, quoted by Hunermann (footnote 23)

thorax, and that its descent may be incomplete until because of gradual growth or because of hemorrhage into the intrathoracic portion no portion of the growth can pass into the cervical region. When an intrathoracic goiter is present in a child it is usually the result of an increase of aberrant thyroid tissue derived from accessory thyroid tissue carried into the mediastinum with the aortic portion of the thyroglossal duct. The age incidence in the series here reported (table 1) shows an identical incidence at the two extremes of life and the maximum incidence in the sixth decade.

Sex—In our series the incidence of intrathoracic goiter in women 76 per cent, was markedly greater than in men, in whom it was only 24 per cent. These percentages correspond fairly closely to those for the sex incidence in our cases of hyperthyroidism and simple goiter.

TABLE 1—*Age Incidence in Cases of Intrathoracic Goiter*

Age	Percentage
Under 20 years	5
20-30	6
30-40	15
40-50	22
50-60	27
60-70	20
70-80	5

ETIOLOGY

The thyroid gland is a median extension downward from the same anlage as that from which the tongue is derived, the thyroglossal duct becoming eliminated in the process of development. This downward growth is joined by cells coming from the postbranchial bodies which later fuse and unite with it. In its final form, it consists of two lateral lobes joined by the isthmus. Small, detached portions of thyroid tissue occasionally are found along the course of the thyroglossal duct and are called accessory thyroid glands.

The aortic portion of the thyroglossal duct may also carry accessory glands into the mediastinum, and if these become enlarged, an intrathoracic goiter results. If a cervical thyroid gland becomes enlarged later an intrathoracic goiter may result, the following factors favoring its formation: (1) the anatomic arrangement of the muscles of the neck and (2) deglutition.

The sternothyroid muscle is attached to the posterior surface of the sternum and thus affords a smooth surface for the gland to slip over in entering the thorax and because of the resistance offered by the anterior group of muscles in the neck descent into the thorax becomes the path of least resistance. Posterior growth is limited by

the trachea, and lateral growth by the scalenus and sternomastoid muscles. Deglutition also tends to favor the downward growth of the tumor.

After the goiter—which in these cases is usually a colloid adenoma or a cyst—passes into the thorax, it may gradually increase in size, or, in rare cases, increase suddenly because of a hemorrhage into the cyst, the goiter becoming so large that it is unable to pass back through the aperture into the cervical region, it thus becomes fixed in the thorax. Terry also mentions the influence of gravity and the dragging effect of inspiration as factors in the etiology of intrathoracic goiter.



Fig 9—Photograph of patient with intrathoracic goiter showing engorgement of veins over chest

SYMPTOMS

The symptoms of intrathoracic goiter may be divided into two groups: the subjective and the objective. They may be classified also according to the changes in the respiration and circulation and the alterations in adjacent structures which are produced by pressure.

The most important subjective symptoms are dyspnea, hoarseness, coughing, change in voice, stridor, dysphagia and symptoms of hyperthyroidism.

The dyspnea is usually continuous and is frequently associated with an inspiratory stridor. It was present in 66 per cent of the cases in our series. Because of this symptom a mistaken diagnosis of

asthma is sometimes made, as had happened in four of these cases. Choking occurred in 30 per cent, being more pronounced when the patient was in the recumbent position because of the resultant increased pressure on the trachea. Dyspnea and choking are usually more pronounced when the goiter is in the median line and presses directly on the trachea.

Dysphagia due to pressure, was present in some degree in 24 per cent of the cases. In seven cases this symptom was marked and was constantly increasing in severity while in the other cases it was only moderate and intermittent.

Hoarseness and change in voice were present in 25 per cent of the cases. The onset of these symptoms had usually been insidious and the symptoms were more pronounced in cold, damp weather and in the morning. In some cases, the voice seemed more impaired when patients were in the recumbent position and the hoarseness tended to clear up during the day.

A few patients complained of coughing. This symptom is due either to irritation of the trachea by pressure or to irritation of the recurrent laryngeal nerves.

A moderate degree of stridulous breathing was present in 7 per cent of the cases, the onset of this symptom having been gradual. It was marked in two cases, in one of which bilateral abductor paralysis was present.

Headache, usually temporal and occipital, was present in 57 per cent of the cases.

Some symptoms of hyperthyroidism were present in many of the cases in this series. Although the complete clinical picture of the disease was not present, a sufficient number of the typical symptoms were observed to justify their classification as cases of hyperthyroidism. Tachycardia was present in 53 per cent of the cases, the rapid action of the heart having been noticed by the patient. In 27 per cent the pulse rate was above 130, in 12 per cent, between 120 and 130 and in the remainder, between 90 and 110. Nervousness was present to some degree in 61 per cent, in 27 per cent this symptom was very noticeable, in the others it was mild or present only at intervals. A loss of weight had been noted in 43 per cent of the cases, the loss averaging between 8 and 14 pounds (3.6 and 6.4 kg). In 37 per cent a considerable degree of tremor was present, this symptom having been observed by the patient in the majority of the cases, often because of the resultant difficulty in writing. Exophthalmos occurred in 8 per cent of the cases. No cases of unilateral exophthalmos were observed but unequal exophthalmos was noted in some cases. The basal metabolic rate was not determined in all the cases in which the symptoms of hyperthyroidism were observed but in those in which estimations were made the average rate was ± 32 per cent.

The foregoing figures demonstrate that the absence of a palpable thyroid gland does not rule out the possibility of hyperthyroidism. Therefore when symptoms of hyperthyroidism are present and a gland cannot be palpated, a roentgenogram of the chest should be made to determine whether or not an intrathoracic goiter is present. In such a case, special care should be taken to avoid a mistaken diagnosis of neurocirculatory asthenia. In one of our cases a thyroidectomy had been performed some time before. The basal metabolic rate at the time of examination was $+57$ per cent. An operation was performed

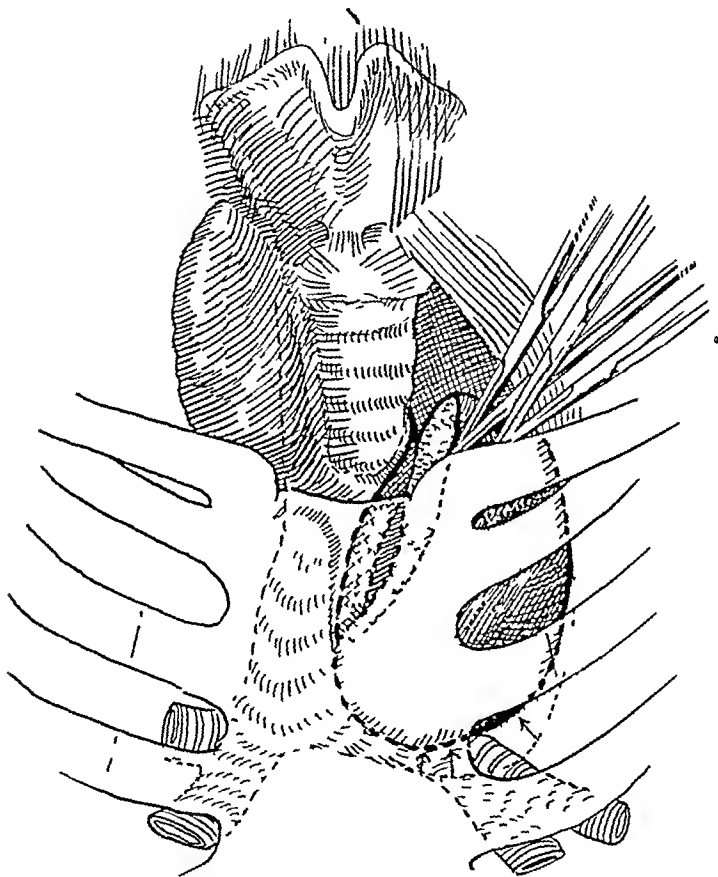


Fig 10—Schematic drawing showing technic of mobilization of the gland

and a large intrathoracic goiter was removed. One month later, the basal metabolic rate had dropped to $+11$ per cent.

In 13 per cent of the cases, there was evidence of preoperative paralysis of the recurrent laryngeal nerves, in 12 per cent, the left abductor was paralyzed, and in one case there was a bilateral abductor paralysis. Adductor paralysis has not been observed in any of the cases in this series. Because of the gradual involvement of the recurrent nerve, a tracheotomy has not been required in any case, this might have been necessary if the nerve had suddenly become involved. The more frequent involvement of the left nerve is difficult

to explain. The difference in the anatomic position of the recurrent nerves may have some bearing on this question. When one recalls that the left nerve springs from the vagus as it crosses the aortic arch, and, after passing around the arch, passes upward in the superior mediastinum between the trachea and esophagus, reaching the neck through the tracheo-esophageal groove, it would seem that its longer course might cause it to be more subject to trauma than is the shorter right nerve.

As the result of pressure on adjacent vessels, obstruction of the superior vena cava may occur, causing the venous blood to return by collateral channels and the vessels of the chest to become enlarged, engorged and prominent. In some cases the jugular veins are much distended, and extreme distention of the veins on the anteriolateral portion of the chest and abdomen becomes evident. The lips and face may also become cyanosed.

TABLE 2—*Duration of Symptoms of Intrathoracic Goiter*

Duration	Cases
6 months-1 year	19
1 year-5 years	22
5-10 years	20
10-20 years	21
20-30 years	8
30-40 years	5
40-50 years	2
Over 60 years	30

Dittich has reported a difference in the width of the pupils in cases of intrathoracic goiter, presumably caused by pressure on the sympathetic nerves. This phenomenon was present in two of our cases.

Inequality of the radial pulse, due to pressure on the subclavian artery, may also occur, but this was not observed in any of our cases.

Duration of Symptoms—In determining the duration of the symptoms, every effort was made to secure accurate information, with the results given in table 2.

It is evident that among these cases are some in which the patients had had symptoms as long as they could remember.

DIAGNOSIS

There are several conditions the differential diagnosis of which should be borne in mind in any case in which the presence of an intrathoracic goiter is suspected, namely, Hodgkin's disease, mediastinal tumor, asthma, tuberculosis, mediastinitis, aneurysm of the aorta, persistent thymus, abscess of the lung and pneumonia.

As mentioned previously, four of the patients in this series had been treated for asthma as the result of a mistaken diagnosis. A

roentgenogram would have revealed the real cause of the trouble in these cases but owing to the fact that no toxic symptoms were present and only mild symptoms of pressure a roentgen-ray examination was not made

Hodgkin's disease can usually be ruled out by a careful history and examination for multiglandular enlargements and the clinical diagnosis may be substantiated by biopsy

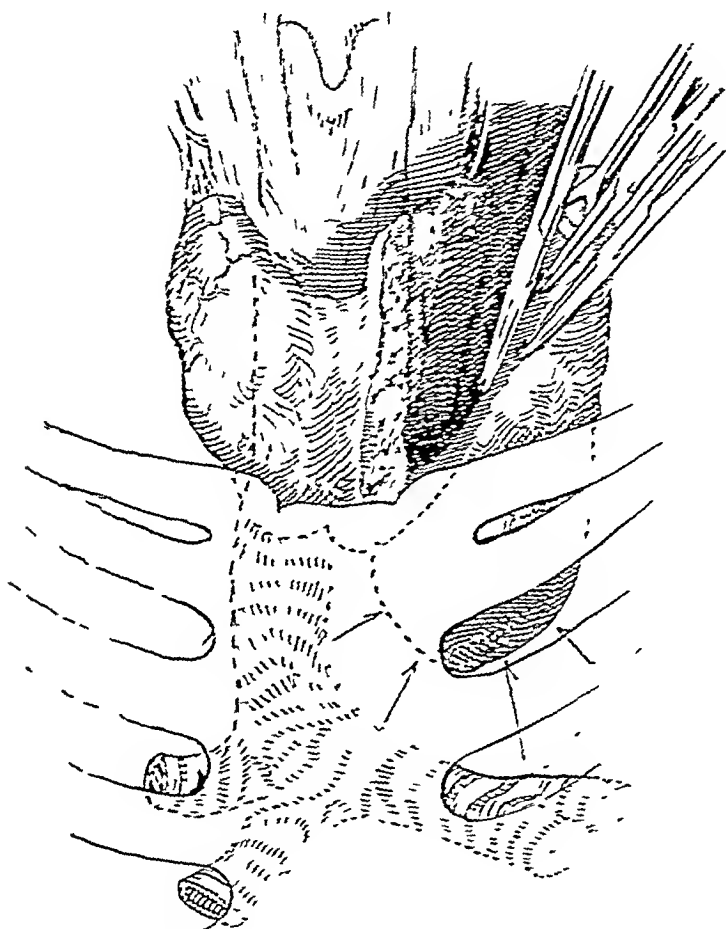


Fig 11—Schematic drawing showing technique of mobilization of the gland

A persistent thymus usually occurs in a child. A careful history and roentgen-ray examination will usually rule out this condition. The possibility of a mediastinal tumor can also be ruled out by roentgen-ray examination. It may be difficult to differentiate between intrathoracic goiter and aortic aneurysm but a careful history, a Wassermann test and roentgen-ray studies will establish the diagnosis.

The diagnosis of abscess of the lung and of pneumonia is easily established by the history, the physical signs and roentgen-ray examination. An esophageal diverticulum can be diagnosed by the history, and by means of a barium meal the roentgenogram revealing a dilated pouch connected with the esophagus.

Roentgen-Ray Examination—The roentgen-ray examination should include stereoscopic roentgenograms in the anteroposterior and oblique positions, a fluoroscopic examination is also of value in differentiating between an intrathoracic goiter and an aortic aneurysm. A distinct angle is usually present between the aortic shadow and that of the intrathoracic goiter, a point which has been brought out by Crotti; this angle changes during inspiration and deglutition because of the ascent and descent of the goiter. This is an important observation in establishing the differential diagnosis, as is also a deviation or a deformity of the trachea.

PATHOLOGY

In the majority of cases of intrathoracic goiter a colloid adenoma is present. A complete intrathoracic goiter is rarely found to be a hyperplastic gland. In this series the pathologic reports showed the following conditions: fetal adenoma, sixteen cases; cystic colloid ade-

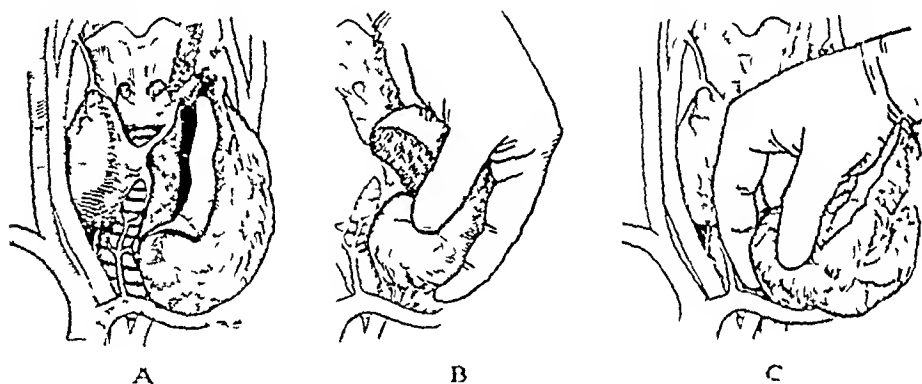


Fig 12—Complete mobilization of intrathoracic lobe

noma, twenty-seven cases; colloid adenoma, thirty-three cases; colloid goiter, twenty-one cases; and hyperplasia, three cases.

In the majority of the cases in the series—69 per cent—the goiter was on the left side, it was on the right side in 35 per cent. In 6 per cent it was bilateral.

TREATMENT

Surgical intervention alone is of avail in the treatment of patients with intrathoracic goiter. If the operation is performed at an early stage when the tumor can easily be delivered into the neck, it is a safe procedure. The surgical mortality in the cases in this series has been only 1 per cent. A transverse division of the sternothyroid and sternohyoid muscles is rarely necessary. Evacuation of the contents of an intrathoracic goiter by morcellation is attended by hemorrhage and should be avoided.

Technic—After securing an adequate exposure which in some cases necessitates a transverse division of the prethyroid muscles the

upper pole of the gland is first freed from the trachea, to facilitate mobilization of the goiter, and the superior thyroid vessels are clamped and ligated. The thyroid is then freed downward from the trachea, care being taken to point the hemostats outward in order to avoid injury to the recurrent nerves. This dissection is continued until the entire upper pole is mobilized. The bleeding points are then ligated before an attempt is made to deliver the intrathoracic portion of the

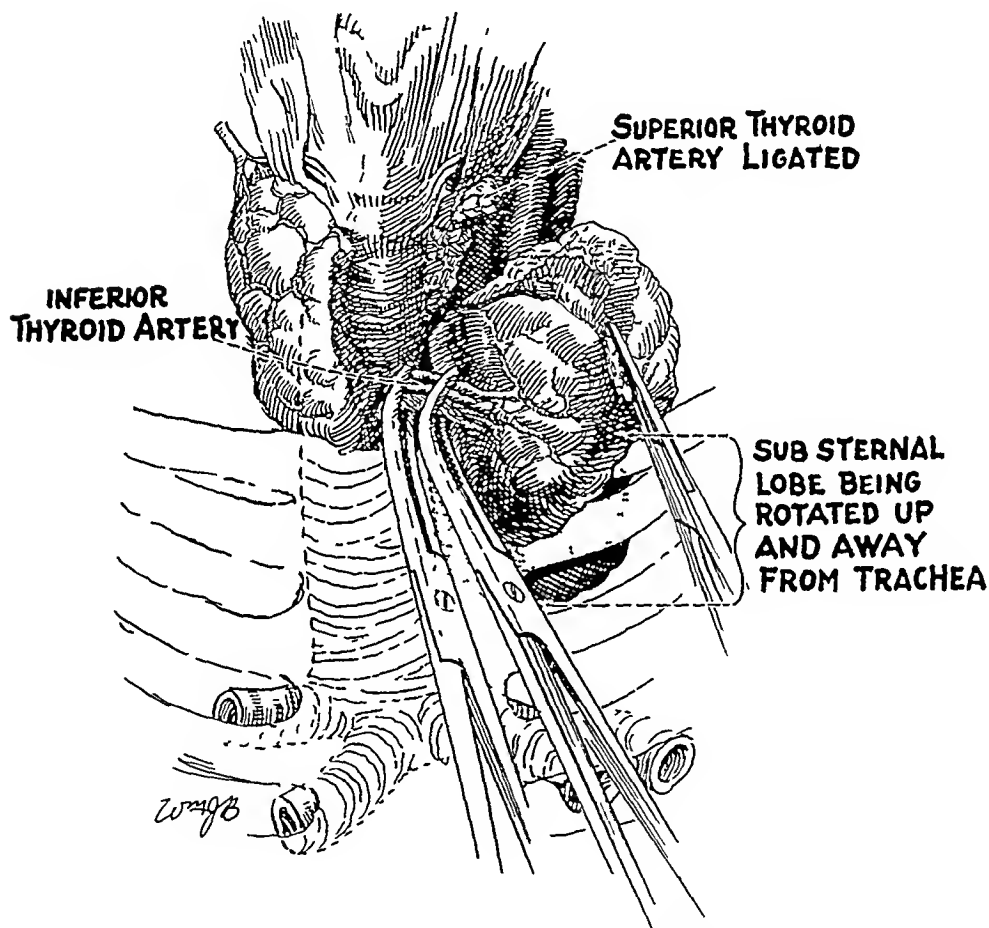


Fig 13—Location of inferior thyroid artery

goiter. In this way the field is kept clean, and there would be no obstruction by hemostats should an emergency arise.

After the cervical portion of the gland has been completely mobilized, the finger can be passed down about the tumor, care being taken to avoid getting outside its fibrous capsule, and the tumor can be delivered into the neck. It is surprising how mobile the goiter becomes after the upper pole of the gland is freed from the trachea. It must be remembered always that the tumor is in close proximity to important structures and that the greatest caution must be used in delivering it.

The lower pole is then ligated. Ordinarily, arterial circulation enters the lower pole through the inferior thyroid artery which communicates with the gland halfway between the poles and remains in the same location regardless of the position occupied by the goiter. After adequate hemostasis has been secured, a tape should be placed in the cavity to prevent rupture of the pleura or oozing into the mediastinum, and the incision is held open with iodoform gauze. The tape should be removed at the end of twenty-four hours. A catheter can then be placed in the cavity in order to remove the serum by aspiration, the muscles can be reapproximated and the incision closed with clips, thus allowing the catheter to emerge through the center of the incision.

SUMMARY

1 Complete intrathoracic goiter is a relatively uncommon condition, the incomplete type being more frequently observed.

2 In cases in which the presence of an intrathoracic goiter is suspected, roentgen-ray examination should be made to rule out other conditions which may produce similar symptoms. In cases in which symptoms of hyperthyroidism are present and the thyroid gland is not palpable, roentgen-ray examination is indicated.

3 Surgical treatment alone can relieve the symptoms of intrathoracic goiter and early operation is urgently advised. The surgical mortality can be kept to a minimum by careful management of the patient and by the avoidance of hemorrhage and of injury to adjacent structures.

PNEUMOCEPHALUS OF BACTERIAL ORIGIN*

WALTER E DANDY

BALTIMORE

Intracranial air occurring during life may arise from two possible sources (1) it may be forced through a break in the cranial bony and meningeal coverings overlying the air spaces, or (2) it may be a product of microbic origin. In a recent article of mine¹ the various aspects of pneumocephalus were considered at length, but my knowledge of this condition was then restricted to the first variety, in which the air was forced through an opening to the exterior. A case was presented, however, in which air was roentgenologically demonstrated in a cranial abscess, but the source of the air could not be absolutely determined. Although the air of bacterial origin was then considered a possibility, it was concluded, for reasons none too convincing when reviewed in retrospect, that more probably the air had entered through a break in the dura which was known to be present and through which pus was discharged intermittently when the dura was elevated. Unfortunately, the bacteriologic proof of the character of the organism was lacking.

At the time of the first publication I was not able to find in the literature any report of a case in which intracranial air of microbic origin occurred during life. This note is essentially a supplement to the first article. It presents a recent example of intracranial air arising from bacteria and assembles from the literature the reports of three other cases which escaped my notice at that time.

REPORT OF AUTHOR'S CASE

History—A boy, aged 6, was ready to be discharged from the hospital one week after a mastoid operation (performed a week previously) when fulminating signs of intracranial pressure suddenly developed. Except that there had been intermittent discharge from both ears for the past four years, his past history was not significant. Three weeks before his admission to the Johns Hopkins Hospital, the discharge reappeared in the right ear. One week later, the soft tissues back of the right ear became swollen. This swelling gradually increased and became progressively more painful. Fever and chills had been present during the week before admission. When the mastoid operation was performed by Dr Snelling, the dura was exposed, it was covered by granulation tissue, but there seemed to be no evidence of perforation. One week later, the patient complained of severe headache, and during the day he vomited several times. The pulse rate changed from 120 to 64 in less than twenty-four hours. There was marked papilledema in both fundi, the temperature remained unchanged and normal. An abscess in the temporal lobe was suspected because of the underlying mastoid infection.

* From the Department of Surgery, Johns Hopkins University.

1 Dandy, W E. Pneumocephalus, Arch Surg 12 949 (May) 1926.

Treatment—Through a perforator opening beneath the temporal muscle, an abscess was immediately encountered by a puncture with a ventricular needle. An ounce or more of foul-smelling pus escaped. A week later intracranial pressure had returned, and again it was necessary to tap the abscess. Many bubbles of gas were then seen to spurt through the pus in the needle. A roentgenogram revealed a large round shadow of air in the temporal lobe. The intracranial pressure then returned so quickly that it was necessary to evacuate the abscess every two days and finally every day. The amount of gas became greater with each tapping, and the amount of pus both relatively and absolutely less (the intervals of time, of course, were growing shorter). As the infection was gaining the upper hand under intermittent tapplings, a small rubber tube was inserted into the abscess cavity. Continuous drainage continued for five days after which the tube was withdrawn and a protective wick inserted. Drainage ceased a few days later. Six weeks after the abscess was first tapped, the roentgenogram showed no shadow of air, and a week later the patient was discharged as well.



Fig 1—Roentgenogram (lateral view) showing collection of air (of bacterial origin) in an abscess of the temporal lobe

One year later, the patient was still well in every respect. He had never had contralateral motor or sensory changes and no convulsions. The only symptoms at any time during his illness were those of intracranial pressure. Cultures were completely studied by Dr. Amoss in the bacteriological division of the medical clinic, but the organism which produced the gas could not be identified. He reported a heavy growth of gram-negative bacilli, dextrose and maltose fermented with production of gas. The organism was non-motile, non-spore-bearing and did not grow aerobically. Clearly, it was not *Bacillus aerogenes-capsulatus* of Welch. *Streptococcus zindans* also grew from the cultures of the abscess.

REVIEW OF THE LITERATURE

As mentioned before, I had been unable to find reports of similar cases when my article on pneumocephalus was published. Reports of three cases have since been found: one reported by Bier² and two by

² Bier. Anaërobe Wundinfektion. Beitr. z. klin. Chir. 101:271, 1926.

Rychlik³ All followed wounds of the head Bier's patient died five days after a severe compound wound of the vault of the skull Bubbles of gas were seen exuding with pieces of necrotic brain tissue Necropsy was performed half an hour after death, but no mention was made of the cerebral abscess Purulent meningitis was doubtless the cause of death Although cultures were not made, Aschoff, who conducted the autopsy, considered the organism to be *Bacillus aerogenes-capsulatus* Roentgenograms of the skull were not made

Rychlik's cases were much more impressive His first patient was only slightly injured by fragments of grenade Consciousness was not lost, but on the following day he was sent to the hospital On the third

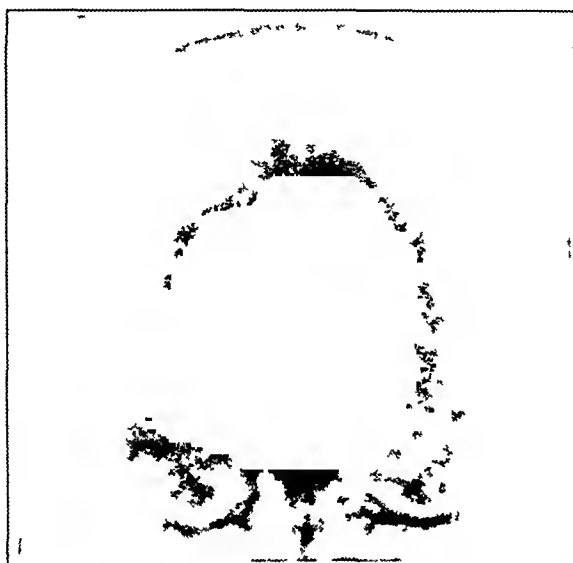


Fig 2—Roentgenogram showing collection of air (same case) in anteroposterior view

day his temperature rose to 39 C (102.2 F), but the cause was first suspected on the fifth day, when headaches developed, as they were not severe, however, it seemed possible to explain them on the basis of his high fever On the sixth day the left side became paralyzed Bilateral papilledema was also present An abscess was found in the frontal lobe, and the opening was enlarged with a finger A second, smaller abscess in the temporal lobe was detected by the finger The abscess drained several weeks The patient was cured From the cultures of the abscess the gas bacillus (*B. welchii*) was grown in pure culture Apparently animals were not injected with cultures of this organism Roentgenograms were not taken

³ Rychlik, E Gasabszess des Gehirns, Munchen med Wchnschr 63 1713, 1916

As an appendix to this article, Rychlik adds a brief note of a second similar case. Two days after being injured by a grenade splinter, the patient developed severe headache and a temperature of 39 C. A frontal abscess was drained, and the patient recovered. Gas bacilli were grown in pure culture, no inoculations were made, nor were roentgenograms taken.

Probably the most surprising fact which has appeared from a study of these aerogenic infections is the low mortality under proper treatment, and in two of them (Rychlik's cases) the organism is the dreaded *Bacillus aerogenes-capsulatus* of Welch. The evidence is too meager to draw any conclusions about the outcome of Bier's case, in fact the evidence presented is not sufficient to indicate that the air was of bac-



Fig. 3—Photograph showing healed wound after drainage of air containing abscess (of bacterial origin)

terial origin. It may well have been forced through a bony defect of a frontal air sinus.

Although the organism in my case must remain unidentified, careful studies have eliminated the gas bacillus. Were it not for the fact that the organism has been shown to be gram-negative and non-spore-bearing, it might well have passed as a gas bacillus. The clinical behavior is not unlike that in Rychlik's case, in spite of the fact that the organisms may be different.

It seems incredible that the gas bacillus (of Welch), which causes such havoc when attacking other parts of the body, should be so innocuous in the brain. In my case there were never signs of illness other than those of intracranial pressure. On one occasion the patient's temperature rose to 102.6 F (probably an index of pressure) but with

the exception of this brief elevation, the temperature ran at a fairly uniform level around 99 to 99.5 F. As soon as the intracranial pressure was relieved, he was playful and gave no impression of being sick, and in this respect both of Rychlik's cases are essentially the same. There can be no doubt that without drainage of the abscess all these patients would have died. Although I have been treating patients who have cerebral abscesses by simply evacuating the abscess instead of by continuous drainage, it was necessary in this case to resort to continuous drainage, for the rate of production of gas was soon overwhelming.

I have also been impressed with the failure of these infections to spread, as they are wont to do in other regions of the body. On the contrary, all have been isolated and have become well walled off. Rychlik mentions a second small abscess contiguous to the main abscess, but it drained satisfactorily through the common portal of exit.

Multiple gas abscesses of the brain have frequently been described in postmortem specimens. There has been no clinical proof, however, to indicate that these conditions have been of antemortem origin. In fact, it is well known that after death gas-forming bacilli take on new and unbridled growth, and this knowledge has caused the impression to prevail that these abscesses are all of postmortem origin. At least it remains to be proved that they are of antemortem formation.

SUMMARY

1. A case of pneumocephalus of microbial origin is reported. Two and possibly three other cases have been collected from the literature.

2. In three of these cases the organisms had formed cerebral abscesses. Though two were presumably caused by *Bacillus aerogenes-capsulatus* of Welch, they were isolated and well walled off. In my case the organism was not the bacillus of Welch. Though its characteristics have been carefully studied, its exact identity remains obscure.

3. In these cases there were almost no systemic symptoms due to the organism. The symptoms and signs were almost extensively those of intracranial pressure.

4. All of the patients were cured by continuous drainage.

INJECTION OF ABSOLUTE ALCOHOL IN THE TREATMENT OF HYPERTHYROIDISM *

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AND

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Experimental observations made by one of us (H B B) ¹ on the effect of the injection of absolute alcohol into the thyroid gland showed a local coagulation necrosis, the extent of which varied directly with the amount of alcohol injected. No general effect was observed. The experiments warranted the conclusion that the injection of absolute alcohol in suitable quantity in cases of disease of the thyroid is a safe and legitimate method. Following this conclusion, we have used this method of treatment in severe hyperthyroidism, and in this paper we report the results.

The use of multiple more or less minor operative procedures in preparation for subtotal thyroidectomy in severe cases of hyperthyroidism is well recognized. Though the use of compound solution of iodine as advocated by Plummer ² has made it possible to convert many cases of exophthalmic goiter from poor risks to the class of fair risks or good risks, there remains a group of patients who do not respond sufficiently to medication to be satisfactory risks for subtotal thyroidectomy. In addition to these cases of exophthalmic goiter, there are cases of adenomatous goiter with marked hyperthyroidism and cardiac damage in which multiple procedures must be used in order to produce fair operative risks for eventual subtotal thyroidectomy. Any procedure which promises benefit and can be carried out with little risk to the patient is worthy of trial in these cases. Porter ³ and Crile ⁴ have emphasized the importance of the use of multiple procedure in the preparation of these patients for thyroidectomy. It is admitted that erring on the side of safety is the only practice that will prevent a high mortality in these types of cases. The minor procedures in common use

* From the Department of Surgery, University of Michigan.

1 Barker H B. The Injection of Absolute Alcohol into the Thyroid Gland, Arch Surg 2 180 (Aug) 1925

2 Plummer H S. Results of Administering Iodine to Patients Having Exophthalmic Goiter. I A M A 80 1955 (June 30) 1923

3 Porter, M F. Injection of Boiling Water in the Treatment of Hyperthyroidism. I A M A 61 88 (July 12) 1913

4 Crile G W. The Thyroid Gland. Philadelphia W B Saunders Company, 1922

are ligation of the superior or inferior vessels, methods of injection, removal of small portions of the gland and the introduction of radium suggested by Terry⁵

Many substances have been injected into enlarged thyroids for the purpose of destroying part of the gland. The literature concerning this procedure has been reviewed in a previous report¹. The substances generally used for this purpose are boiling water, as advocated by Porter,⁶ urea and quinine sulphate, as proposed by Watson,⁷ and a solution of phenol, iodine and glycerine, as used by Sheehan.⁸ By far the most popular of these methods has been that of Porter, which, however, offers technical difficulties. Experiments by Barker¹ with many nontoxic solutions suitable for the purpose showed that absolute alcohol met all the requirements of a nonpoisonous coagulant to the thyroid, and it has been used on a series of patients with extremely toxic goiter, after all other methods had failed to cause sufficient improvement to allow a subtotal thyroidectomy without too great a risk.

In the experiments on animals, quantities of absolute alcohol of from 0.5 to 10 cc were injected into the thyroid glands of dogs, and the glands were removed at intervals varying from fifteen minutes to two months. In these thyroids, coagulation necrosis was produced and, in turn, was replaced by fibrous scar tissue. The following technic was used for the injection of alcohol.

TECHNIC

The technic used for making injections into patients with goiter was that used in dogs, except that the injections were made under local anesthesia. A 2½ inch (6.27 cm), 0.22 Luer needle and a 10 cc Luer syringe were used for the injection of the alcohol, and a 1 inch (2.5 cm), 18 bore needle was used for introducing the local anesthesia. A small wheal was raised in the skin by the injection of 1 per cent apothesine. This wheal was placed lateral to the median line of the body over the median line of the lobe in which the injection was to be made. The fingers of the left hand were next placed behind the sternomastoid muscle and the lobe, lifting the lobe anteriorly and medially. The small needle was introduced into the wheal, and a tract from there to the gland was infiltrated with the solution of apothesine. The large needle was then introduced along this tract into the gland. During the introduction of the needle and also during any subsequent movement of the needle in the gland, it was necessary that the needle be free from the syringe or any obturator so that bleeding would give evidence of the presence of large veins, and the alcohol would not be injected directly

5 Terry, A. I. Radium Emanations in Treatment of Goiter, *J. A. M. A.* **76** 1821 (June 25) 1921.

6 Porter, M. F. Boiling Water Injections into the Thyroid Gland for Hyperthyroidism, *Surg. Gynec. Obst.* **21**, 1915.

7 Watson, L. F. Injection of Quinine and Urea Hydrochloride in Hyperthyroidism, *J. A. M. A.* **62** 126 (Jan 10) 1914.

8 Sheehan, J. E. Seventeen Cases of Goiter Treated with Injections of Carbolic Acid, Iodine and Glycerin, *M. Rec.* **92** 591 (Oct 6) 1917.

into the circulation. The injection needle then entered the midportion of the lobe and was introduced well into its substance. It can easily be demonstrated that the needle is engaged in the gland by having the patient swallow the skin acting as a fulcrum, while the long arm of the lever, the base of the needle, moves up and down (fig 1 C). An obturator should be introduced into the needle before an injection is started to avoid blocking caused by the coagulation of blood and thyroid substance collected in the point of the lumen during its introduction. The desired amount of absolute alcohol was then introduced. The syringe was disconnected, the needle advanced about 2 cm toward either pole and more alcohol was introduced, the process being continued until the lobe was satisfactorily infiltrated. The largest quantity of alcohol injected at one sitting was 30 cc.

RESULTS

In no case was an immediate or remote ill effect from the alcohol observed. On the day following the injection, and continuing until the third or fourth day, there was a rise in temperature and local evidence of aseptic reaction. The gland was increased in size and this increase

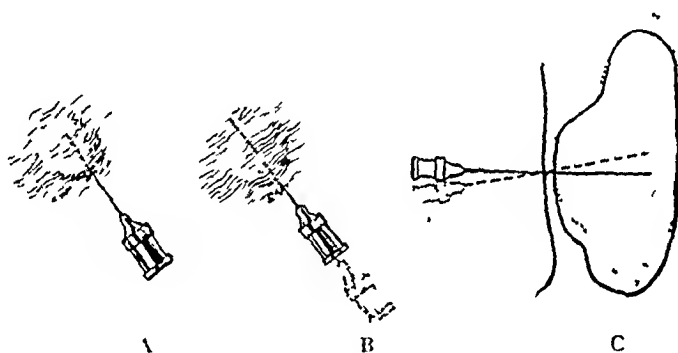


Fig 1—*A*, introduction of anesthetic, raising wheel, *B*, anesthetizing soft parts over gland, *C* shows movement of needle during act of swallowing, this confirms the fact that the needle is in the gland

subsided more slowly than the other evidences of local reaction. The enlargement was not sufficient to cause respiratory embarrassment from tracheal compression, nor was there any interference with the function of the recurrent laryngeal nerves.

Severe pain did not result from the injection in any case, although some patients complained of a sharp pain "like a toothache" back of the ear while the upper pole was being infiltrated. This lasted but a few moments. In one case pain was referred to the inferior mandibular division of the fifth cranial nerve on the side on which the injection was made. Most of the patients had several injections at varying intervals. The question of the amount of infiltration of the gland to be accomplished at a sitting must be decided by the condition of the patient. We have made injections into both lobes at one sitting in some patients.

and into only one lobe or a portion of a lobe at one time in others. The process can be carried on indefinitely, if one wishes to do so until the gland is reduced to a scar.

In the cases in which operation was performed, special care was taken in the microscopic study of the section to determine the effect of the injections. Since in some of them injections had been performed several times at long intervals, it was possible to contrast the changes from recent injections with those of earlier ones. The microscopic observations on these glands were similar to those made on the experimental animals. There was coagulation necrosis followed by a round

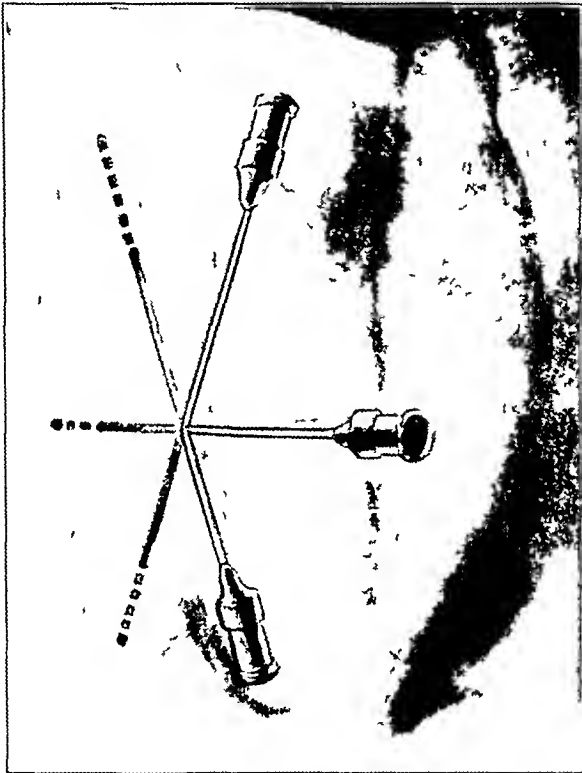


Fig 2—Position of needle during injection in different parts of the gland

cell infiltration and fibroblastic proliferation and organization. Foreign body giant cells were found about bits of colloid which had been acted on by the alcohol, producing the reaction of a foreign body. The ultimate picture was one of fibrous tissue replacement of the destroyed thyroid tissue. The blood vessels passing through the injected area showed thrombosis, and in older areas organization of the thrombus with canalization. When numerous injections had been made, this factor alone must have meant considerable decrease in the blood supply of the gland.

The single objection to methods of injection is that the ultimate operative procedure is made more difficult by pericapsular adhesions.

These were more marked in the cases in which large amounts had been injected at one sitting and were less marked in those in which there had been repeated injections of small quantities. This observation fits well with the experimental observation that the alcohol tends to leak out of the thyroid capsule around the injecting needle after the intracapsular pressure has been sufficiently raised. We believe that the technical difficulties of subtotal thyroidectomy will not be greatly increased by the injection of small quantities of alcohol on repeated occasions rather than a single large injection. We advise injections of from 8 to 16 cc. to a lobe repeated at weekly intervals, the number of injections being determined by the size of the gland.

ABSTRACT OF CASES

CASE 1—History—Mrs. B. M. L., aged 19, a clerk, entered the medical service of the hospital on Nov. 10, 1923, complaining of pain over the heart. The family history was unimportant, except that one brother had chorea. The patient had had frequent attacks of sore throat and one attack of rheumatic fever seven years before. Her ankles and knees were involved in this attack, and she was confined to bed for two weeks. She also had had scarlet fever four years before with uneventful recovery. A tonsillectomy had been performed three years previous to admission.

The present illness began with pain over the heart and palpitation fifteen months before she entered the hospital. Nine months before admission, an enlargement of the thyroid, which increased steadily in size, was noticed. This was associated with extreme nervousness and irritability. Jerky movements of the head and hands had been present for about six months before she came to the hospital. Her weight was 152 pounds (69 Kg.) in November, 1922, and at entrance to the hospital 117 pounds (53 Kg.). Beginning in June, 1923, she had received ten treatments with the roentgen ray, and had been given iodine for three months, during this time she was also placed on a low protein diet, and had much rest in bed.

Examination—The patient was well developed, fairly nourished and rather restless, and irregular, jerky movements occurred in all parts of the body. Definite exophthalmos was present. The thyroid was enlarged, more on the right side, and it was of firm uniform consistency. A definite bruit was heard over both lobes but no thrill was felt. The heart was moderately enlarged. A faint systolic murmur was heard in the pulmonic area and a stronger one at the apex. The pulse rate was 130. The blood pressure was systolic 135 and diastolic 70. The extremities were normal except for involuntary, irregular movements. The fingers showed a fine tremor.

Laboratory Examinations—The urine was normal, the blood showed hemoglobin 85 per cent, 4,490,000 erythrocytes, 6,200 leukocytes and a normal smear, the differential count showed a slight lymphocytosis. The basal metabolism rate was 58 per cent. The electrocardiogram showed an inversion of the T waves.

A diagnosis of exophthalmic goiter and chorea was made.

Treatment and Course—The patient was treated in bed until May 24, 1924. During this time she was given roentgen-ray irradiations over the thyroid. The basal metabolic rate varied from the rate at entrance to 70 per cent and fluctuated between this and 40 per cent. During April she had an acute infection of the

throat with acute arthritis of the knees and ankles, which aggravated all symptoms. The heart rate varied between 110 and 150 and was extremely labile.

On May 22, 1924, she was transferred to the department of surgery. She appeared nervous, and occasional choreiform movements were noted. The exophthalmos was now severe. Both lobes of the thyroid were large, and there was a loud bruit and thrill.

Roentgenograms of the chest showed some compression of the trachea by the goiter. The basal metabolic rate was 46 per cent, the average pulse rate was 130. The weight was 105 pounds (47.6 Kg). The urine was normal. The blood showed hemoglobin, 56 per cent, 3,490,000 erythrocytes, and 6,900 leukocytes, with a slight relative lymphocytosis.

During her stay in the surgical ward the patient was in bed, on a 5,000 caloric diet, but she lost 3 pounds (1.4 Kg) during the next week. On May 31, 16 cc of absolute alcohol was injected into the right lobe of the thyroid, following this, there was considerable local reaction, including an increase in the size of the gland with redness and local heat. On June 1, the pulse rate was 160 and the temperature 101.4 F. Both the fever and the tachycardia gradually subsided, and on June 5, the temperature was normal and the pulse rate ranged between 100 and 110. On June 11, the weight was 105 pounds (47.6 Kg). On June 19, the weight was 111 pounds (50.3 Kg), and the patient was symptomatically much improved. On June 30, she weighed 121 pounds (55 Kg), and the pulse was much more stable, about 110 in rate. The basal metabolism was 38 per cent. She was then allowed to be up and about the ward with a rest period of two hours a day in bed. She continued to improve symptomatically, and the pulse rate varied from 90 to 120 with exercise.

On July 25, impacted third molars were removed under nitrous oxide and oxygen anesthesia, while simultaneously 10 cc of absolute alcohol was injected in each lobe of the thyroid. This was followed by a local and general reaction similar to, but less intense than, that at the previous injections. On August 4, she was discharged from the hospital weighing 130 pounds (59 Kg). The basal metabolic rate was 27 per cent, and the average pulse rate, 100. She was advised to continue the high caloric diet and the rest period.

On November 10, the patient weighed 156 pounds (70.8 Kg) and was greatly improved in every way. She was working as a clerk in a store. The pulse rate ranged from 90 in the morning to 120 in the evening after she had worked most of the day.

On December 7, the patient reported that she was feeling stronger, she weighed 159 pounds (72 Kg), and the pulse rate ranged from 90 in the morning to 110 in the evening.

On January 28, 1925, the patient reported that she continued to work. The pulse readings on several consecutive days averaged 74 in the morning and 90 in the evening. The weight was 163 pounds (74 Kg).

On July 1, 1925, she reported that she considered herself perfectly well.

CASE 2—History—Mrs. M. B., aged 52, a housewife, entered the hospital because of weakness, loss of weight and nervousness. She had had an operation for the removal of gallstones and the appendix. The menopause came four years before her admission to the hospital.

Examination—The patient was fairly well nourished, the mental reaction was slow and she was nervous. The pupils were slightly irregular, and moderate exophthalmos was present. The thyroid was symmetrically enlarged, and was smooth and elastic. Thrills or bruits were not noted. The heart and lungs were essentially normal. The abdomen showed an old surgical scar over the superior

part of the right rectus abdominis. There was a marked fine tremor of the extended hands, but the extremities were otherwise normal. Her greatest weight had been 169 pounds (76.7 Kg) six years before. Her weight on entrance was 102 pounds (46.3 Kg). On February 8, the basal metabolic rate was plus 39.5 per cent and her average pulse rate was 112, after ten days' rest in bed.

Treatment and Course—On this date a bilateral superior ligation of the thyroid was done, and a week later the patient was discharged for six weeks. She did not return until May 14, at which time she was somewhat improved but she was still restless. The basal metabolic rate was plus 25 per cent, the average pulse rate, 100, her weight was 106 pounds (48 Kg). On May 16 an alcohol injection was administered, 16 cc was injected into the left lobe, and 6 cc into the isthmus. There was little systematic reaction, her temperature reached 99.8 F and the pulse rate was elevated to 120. This reaction subsided in two days, and the patient was discharged. She returned to the hospital on June 19, at which time she was less nervous. Her weight was 108 pounds (49 Kg), and she had a basal metabolic rate of plus 23 per cent. Eight cubic centimeters of alcohol was injected into the right lobe, and the patient was discharged from the hospital on the following day. On July 22, she returned symptomatically improved, her weight was 110½ pounds (50 Kg), her average pulse rate 100 and the basal metabolic rate plus 25 per cent. Eight cubic centimeters of alcohol was injected into each lobe, the patient was discharged the following day. She returned on October 2, and reported that she had been feeling well for the past two months, was gaining in weight and was almost completely relieved from nervousness. The basal metabolic rate was plus 15.1 per cent, and the average pulse rate, 76. Fourteen cubic centimeters of alcohol was then injected into the right lobe and 10 cc into the left lobe. The patient was again discharged from the hospital on the day following the injection. She was considered cured and was advised that it would not be necessary for her to return to the hospital as long as she continued to gain in weight.

CASE 3—History—Mrs. E. B., aged 36, a housewife, entered the hospital on March 2, 1924, complaining of palpitation and loss of weight. The present illness began in November, 1923, with palpitation on slight exertion. Shortly after this she became nervous, this symptom increased up to the time of admission to the hospital. She believed that her eyes had become slightly more prominent during the two months before entrance to the hospital. Her best weight was 135 pounds (61.2 Kg) in July, 1923, at entrance she weighed 105 pounds (47.6 Kg). Vomiting and diarrhea had not occurred.

Examination—She was extremely nervous, and had obviously lost some weight. Slight exophthalmos was noted. The thyroid was symmetrically enlarged, and a bruit could be heard over the entire gland. There was not any thrill. The lungs were normal, and the heart was not enlarged, but it was overactive. A blowing systolic murmur at the apex was transmitted to the base. Her blood pressure was systolic, 130, diastolic 72. The abdomen was normal. The extremities were normal except for a fine tremor of the fingers. The reflexes were normal. The blood Wassermann reaction was negative and the electrocardiogram was not definitely abnormal. Her blood showed a slight secondary anemia.

Treatment and Course—She was placed in bed and given a high caloric diet and sedatives. On March 16 her weight was 106 pounds (48 Kg), the basal metabolic rate, 52 per cent and her average pulse rate, 100. On this date, 10 cc of absolute alcohol was injected into each lobe. This was followed by a moderately

severe reaction, and on March 19 she went home. On May 14, she returned to the hospital. Her weight was 118 pounds (53.5 Kg), her basal metabolic rate was 38 per cent and the pulse rate averaged 90. The symptoms were much less severe. On May 15, 10 cc of absolute alcohol was injected into each lobe of the thyroid. She left the hospital on the following day. On July 1, her weight was 124 pounds (56 Kg), her basal metabolic rate was 26 per cent and she was much improved. Ten cubic centimeters of absolute alcohol was injected in each lobe, and she again returned home. On August 2, her weight was 136 pounds (61.7 Kg), her basal metabolic rate was 10 per cent and she was entirely free from nervousness, but still had some palpitation on exertion. On September 15, she weighed 140 pounds (63.5 Kg), and considered herself entirely well. She

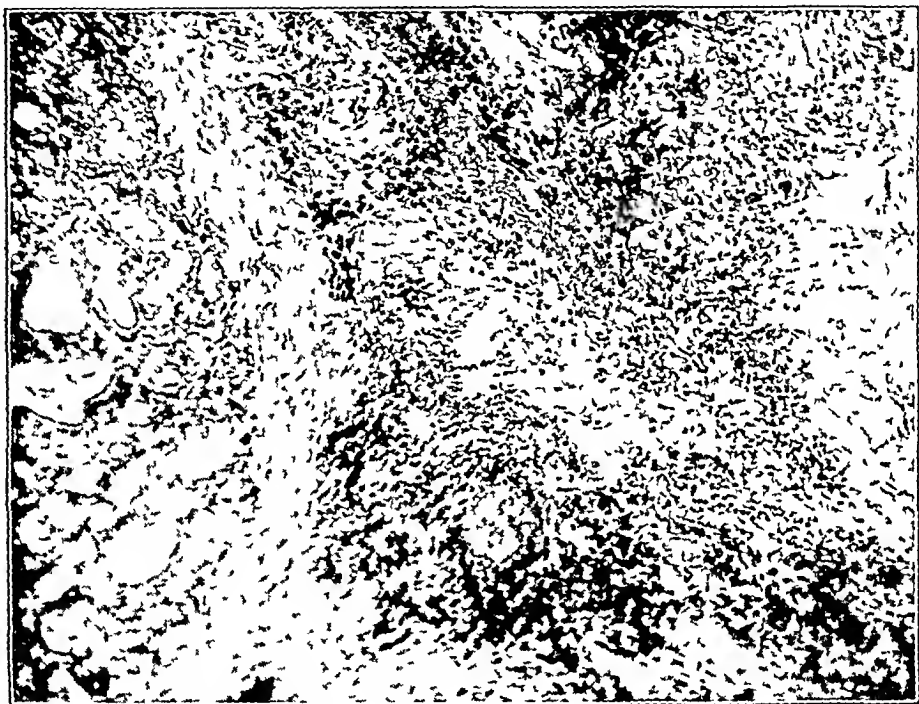


Fig 3 (case 4) —Border of almost completely healed area of necrosis following alcoholic injections

reported by letter in February, 1925, that she was still in what she considered a normal condition.

CASE 4—History—Mrs. O. W., aged 33, a housewife, entered the hospital on Nov. 20, 1923, complaining of enlargement of the neck, nervousness and loss of weight. The patient gave a history of having had some fulness in the neck for eleven years. Her general health was good until three years before, when the neck suddenly began to increase in size and she noticed marked weakness, an increase in appetite and burning and smarting of the eyes. The symptoms had gradually increased, with added prominence of the eyes, extreme nervousness and loss of weight.

Examination—The patient was undernourished. Her skin was warm, moist and somewhat pale. Marked exophthalmos was present. Both thyroid lobes were markedly enlarged, some hard nodules were felt in the gland. Thrill and bruit over the gland and pulsation of the large vessels of the neck were marked. The

heart was somewhat enlarged and overactive. The sounds were normal and regular, the pulse rate was 120. Her blood pressure was systolic 120, diastolic, 60.

The extremities and reflexes were normal. There was a marked fine tremor of hands on extension. Her weight was 97 pounds (44 Kg). The basal metabolic rate was plus 75.5 per cent.

The diagnosis was exophthalmic goiter.

Treatment and Course—The patient was placed in bed on a high calorie diet for three weeks, but she did not improve. On December 13 both superior thyroid vessels were ligated under gas and oxygen anesthesia. There was a moderately severe reaction which subsided in three days. She continued in bed under observation until Jan. 3, 1924, when she was discharged for six weeks. At the time of discharge the basal metabolic rate was plus 75 per cent weight 98½ pounds (44.7 Kg), and average pulse rate, 110.

On March 18, the patient returned to the hospital with an average pulse rate of 110, weight, 98 pounds (44.5 Kg), and basal metabolic rate plus 55 per cent. Her condition was somewhat improved, but she continued to be extremely nervous. The case was not considered a good operative risk. On March 20, 8 cc of absolute alcohol was injected into the left thyroid lobe. A moderate general reaction followed this procedure, the temperature reached 101.5 F., and pulse rate 120. This subsided in three days.

On March 29, 10 cc of alcohol injected into the right lobe resulted in little general reaction, the patient was discharged three days later.

On May 28, the patient returned to the hospital symptomatically much improved. The weight was 112 pounds (50.8 Kg), the pulse rate 90 and the basal metabolic rate, plus 26.2 per cent. The case would have been a good operative risk at this time, but we wished to learn whether further improvement could be made, and whether it would be permanent. On May 31, 14 cc of absolute alcohol was injected into the right lobe and isthmus. A reaction did not occur, and the patient was discharged on June 2.

On July 24, the patient returned, stating that she had been working hard since leaving the hospital early in June. She had lost 13 pounds (6 Kg), and the pulse rate averaged 110. She was more nervous and the basal metabolic rate was plus 65 per cent. Her weight at this time was 109 pounds (49.4 Kg). On July 28, 10 cc of alcohol was injected into each thyroid lobe, the patient was allowed to return home on July 30.

On November 14, the patient returned to the hospital. She had been carrying on her ordinary work without marked symptoms or further loss of weight. Her pulse rate averaged 100, the basal metabolic rate, plus 40 per cent and her weight, 108½ pounds (49.2 Kg). The operative risk was considered good at the time and we felt that the patient would not be able to carry on satisfactorily without a partial thyroidectomy.

On November 24, a subtotal thyroidectomy was performed. Convalescence was uneventful. The pathologic report was 'Nodular goiter with scattered areas of exophthalmic hypertrophy. Colloid on whole fairly abundant.'

In July 1926, the patient returned to the hospital for examination. There was no evidence of hyperthyroidism. The basal metabolic rate was 6 per cent and her weight was 130 pounds (59 Kg).

CASE 5—History—J. D. aged 49, a mechanic was admitted to the medical department of the hospital on Feb. 29, 1924, complaining of weakness, loss of weight and palpitation. In December 1923, he began to lose weight and became weak and nervous. In January 1924 he developed a severe diarrhea which lasted

two weeks. His eyes became prominent. The symptoms increased in severity until the time of his entrance to the hospital. His weight in December, 1923, was 145 pounds (65.8 Kg), and at admission, 116 pounds (52.6 Kg).

Examination—The patient was undernourished and extremely nervous and his skin was moist. The eyes were normal, except for a moderate degree of exophthalmos. There was a bilateral enlargement of the thyroid, more marked on the right, the gland was uniform in consistency, and a definite bruit was heard over both lobes. Both lungs were normal. The heart was slightly enlarged, a blowing systolic murmur was heard loudest in the fourth intercostal space and was transmitted to the base of the heart. The blood pressure was systolic, 128, diastolic, 60. The abdomen was normal, except for tenderness over the right upper quadrant. The genitalia, rectum and reflexes were normal. The fingers

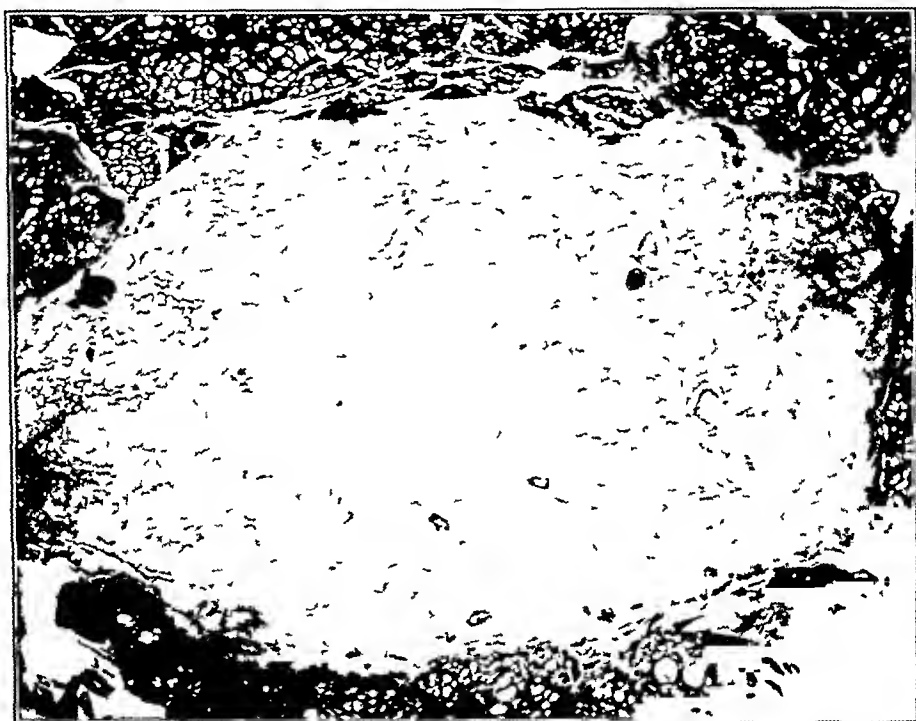


Fig 4 (case 5)—Low power photomicrograph of large area of necrosis in thyroid, localized epithelial hypertrophy and hyperplasia of lymphoid tissue

showed a fine tremor. The basal metabolic rate was 61 per cent, and the pulse rate averaged 108. The electrocardiogram showed ventricular extrasystoles. The urine was normal. An orthocardiogram showed an index of 141 per cent with widening of the aortic arch.

Treatment and Course—Treatment consisted of rest, sedatives and a high caloric diet. On March 15, his basal metabolic rate was 40.5 per cent. At this time, auricular fibrillation was noted, which was present intermittently during his stay in the hospital. On April 7, his basal metabolic rate was 50 per cent and on April 26, it was 42 per cent. During March and April, three roentgen-ray treatments were given.

On May 9, he was transferred to the department of surgery. At this time examinations showed that his condition was about the same as it was at entrance to the hospital, and the patient did not show symptomatic improvement. Auricular fibrillation was still present and his weight was 112 pounds (50.8 Kg).

On May 12, the basal metabolic rate was 51 per cent. On May 13, 6 cc of absolute alcohol was injected into each lobe. No appreciable reaction occurred, and he was sent home on May 15.

On June 16, he returned to the hospital unimproved. The basal metabolic rate was 55.2 per cent, the average pulse rate, 112, and the weight 116 pounds (52.6 Kg).

On June 18, 10 cc of absolute alcohol was injected into each lobe without any reaction, the patient was sent home on June 22.

On September 3, 1924, he returned showing symptomatic improvement. His weight was 124 pounds (56.2 Kg), but the basal metabolic rate which was 53 per cent, and his average pulse rate of 110 did not show improvement. On September 15, a subtotal thyroidectomy was done. The convalescence was uneventful except for auricular fibrillation during the first three postoperative days. The

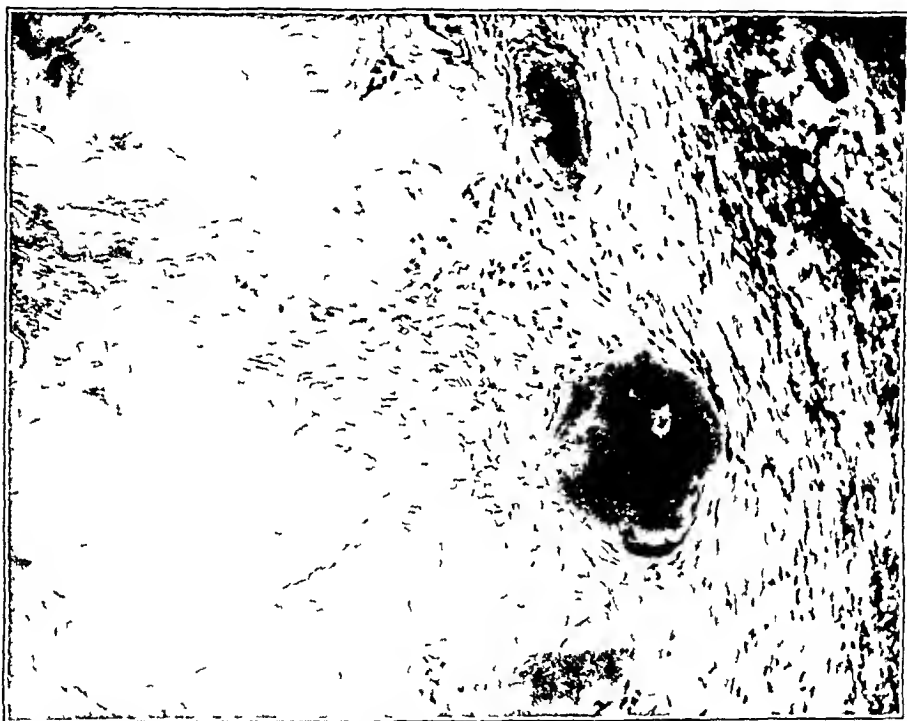


Fig 5—High power detail of border of area of necrosis seen in figure 4, simple necrosis of thyroid acini, surrounded by reactive zone of healing, early encapsulation.

pathologist reported "Tissue weighs 49 grams. There is a marked hyperplasia of the rudimentary lymphoid tissue and areas of epithelial hypertrophy. The picture is that of exophthalmic goiter. There are areas of complete necrosis of the thyroid tissue surrounded by a definite capsule."

He was seen in August 1926 at which time he was in excellent condition. His weight was 147 pounds (66.7 Kg), his basal metabolic rate was 10 per cent and his pulse rate was 80. Exophthalmos had disappeared, and he was free from symptoms.

CASE 6—History—Mrs. E. M., a housewife aged 44 came to the hospital Aug. 29, 1923 complaining of enlargement of the neck, nervousness and loss of weight. In March 1923 she first noticed the nervousness. Since the onset of these first symptoms she had lost 25 pounds (11.3 Kg), and had noticed an

increasing prominence of the eyes. During the six weeks before admission, shortness of breath had been noted.

Examination—The patient was poorly nourished, nervous and irritable. The skin was moist. Marked exophthalmos was present. There was bilateral symmetrical enlargement of the thyroid. A definite bruit could be heard over the gland.

The lungs were normal. The heart was slightly enlarged, the pulse rate was 148, and it was regular. A systolic murmur was heard over the apex and in the mitral area. The blood pressure was systolic 120 and diastolic 60.

The abdomen was normal. There was a fine tremor of the extended hands. Reflexes were present, and were prompt and equal on the two sides. Her weight on admission was 100 pounds (45.4 Kg).

Treatment and Course—On admission to the medical ward, the treatment consisted of rest, a high caloric diet and sedatives.

On September 2, the basal metabolic rate was 78 per cent, and the average pulse rate was 122. On September 18, the basal metabolic rate was 58.5 per cent and the average pulse rate was 116, on September 27, the basal metabolic rate was plus 56 per cent and the average pulse rate was 102.

On October 4, both superior thyroid vessels were ligated, and on October 14, the patient was discharged for six weeks. When she left the hospital, her weight was 92 pounds (41.7 Kg).

The patient returned to the hospital November 2. She weighed 93¼ pounds (42.5 Kg), the average pulse rate was 92, and the basal metabolic rate was plus 36 per cent. It was thought that the patient would make further gain, so she was discharged.

On February 24, 1924, she returned to the hospital with a basal metabolic rate of plus 48 per cent, and an average pulse rate of 112. She weighed 98 pounds (44.5 Kg), and symptomatically had somewhat improved since ligation. During this visit to the hospital, septic tonsils were removed.

On July 18, the patient returned with an average pulse rate of 132, a basal metabolic rate of 61.6 per cent, and a weight of 106 pounds (48.1 Kg). The nervousness was more marked than on the previous visit. On July 22, 12 cc of absolute alcohol was injected into the right lobe and 8 cc into the left. A reaction did not occur and the patient was discharged the following day.

A second alcoholic injection was given on August 15, 8 cc into each lobe. At the time of this injection the basal metabolic rate was plus 51 per cent, the average pulse rate was 115 and the weight was 110 pounds (50 Kg).

On November 18, the patient again returned to the hospital. In spite of the fact that she had been working hard, the basal metabolic rate was lower than on any previous occasion—plus 32 per cent, the average pulse rate was 100 and the weight was 115 pounds (52 Kg). The patient was considered in good condition for operation, and on November 28, subtotal thyroidectomy was done. Convalescence was uneventful. The pathologist reported "Adenomatous colloid goiter with hyperplasia of the rudimentary lymphnodes."

CASE 7—History—Mrs. A. D., aged 38, a housewife, was admitted to the medical service of the hospital on Aug. 31, 1924, complaining of loss of weight and prominence of the eyes.

In January, 1924, palpitation and nervousness were first noticed. In April, her eyes began to be prominent, and they continued to become more so until her admission. Her weight had decreased from 138 to 106 pounds (62.6 to 48 Kg). She perspired freely. In April, the right superior thyroid vessels had been ligated at another hospital without benefit.

Examination—She was fairly well nourished, but showed evidence of loss of weight. The skin was brownish, warm and moist. There was a high grade of exophthalmos. The thyroid gland was symmetrically enlarged and of uniform consistency. A thrill was felt at the superior poles, and a loud bruit was present. The lungs were normal. The heart was enlarged to the left and a blowing murmur, systolic in time, was heard loudest at the apex and faintly in the aortic and pulmonary areas. The average pulse rate was 126, and it was regular. The abdomen was normal. The extremities showed a marked tremor of the fingers and edema of both ankles. The reflexes were normal. The laboratory examinations showed normal urine. The Wassermann reaction was negative. The sugar tolerance test showed a slightly increased fasting sugar and a slight lag in the sugar curve. The basal metabolic rate was 67 per cent. The electrocardiogram showed sinus tachycardia with flat T waves.



Fig 6 (case 7)—Low power photomicrograph of area of hemorrhagic necrosis with border of organization

Treatment and Course—The patient remained in bed on a high caloric diet until October 3. During the early part of this period the patient's symptoms became somewhat less marked, and the basal metabolic rate on September 10 was 51 per cent, and the average pulse rate, 108. After this the symptoms increased in intensity, and on September 26, the basal metabolic rate was 70 per cent, and the pulse rate averaged 126. She was transferred to the surgical service on October 3, when 20 cc of absolute alcohol was injected into each lobe of the thyroid. That evening her temperature was 102.8 F, and the pulse rate was 140. On October 5, the temperature was normal. She was discharged on October 9. Her weight then was 103 pounds (46.7 Kg).

On October 31, she reported by letter that her weight was 116 pounds (52.6 Kg) that the pulse rate averaged 130 and that some edema was present on the ankles.

On November 22, another report stated that there was definite improvement in symptoms. Her weight was 123 pounds (56 Kg) and the average pulse rate was 120.

On Jan 20, 1925, she returned to the hospital. She weighed 138 pounds (62.6 Kg), the pulse rate was from 110 to 120, and there was a definite improvement in symptoms. The basal metabolic rate was 36 per cent. The case was considered a good operative risk, and on January 31, a subtotal thyroidectomy was done. A moderately severe reaction was followed by a normal convalescence. The pathologist reported "Epithelial hypertrophy with marked lymphoid hyperplasia. Larger area of recent necrosis or infarction." Reports received in July, 1926, indicated the patient was well at that time and weighed 160 pounds (72.6 Kg).

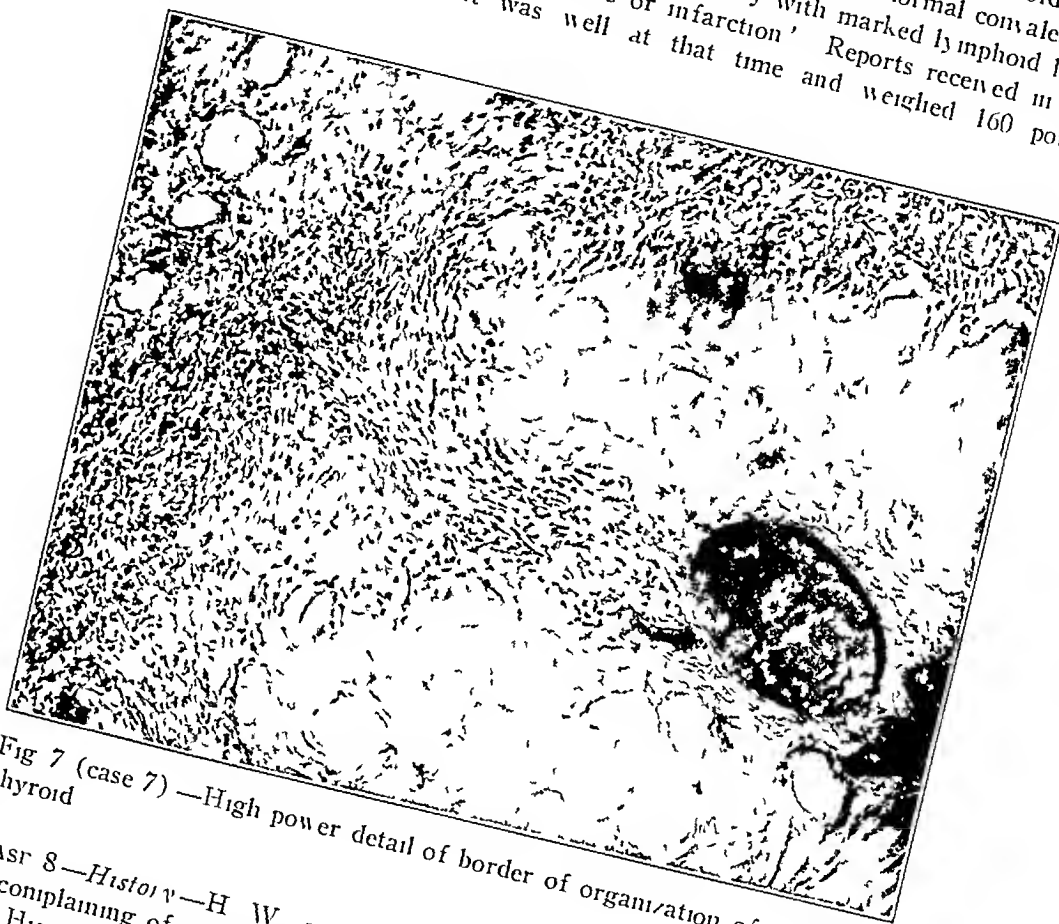


Fig 7 (case 7) —High power detail of border of organization of necrotic area of thyroid

CASE 8—*History*—H. W., aged 50 a farmer, came to the hospital Feb 21 1924, complaining of enlargement of the neck, nervousness and muscular weakness. His present illness began in July 1922, with weakness. This became progressively worse until May, 1923 when enlargement of the neck was noticed. In July, he became nervous and noticed palpitation and his eyes became prominent. In October, he became short of breath. His best weight was 160 pounds (72.6 Kg) in July, 1922 and his weight at the time of entering the hospital was 106 pounds (48 Kg). His appetite was good and there had not been any vomiting or diarrhea.

Examination—He was nervous and undernourished, and presented a severe degree of exophthalmos. The tonsils were hypertrophied. The thyroid was slightly enlarged, more noticeably on the right. There was no thrill but a loud bruit could be heard over the entire gland. The lungs were normal. The heart

was moderately enlarged, with a heaving of the precordium, a blowing systolic murmur was heard at the apex and was transmitted to the base, the pulse rate was 120, and it was regular. The blood pressure was 140 systolic and 60 diastolic. The peripheral vessels were sclerotic.

The abdomen was normal. There was tremor of the extended fingers; the reflexes were active. Laboratory examination showed that the urine was normal. The electrocardiogram showed sinus tachycardia. The basal metabolic rate was 70 per cent. The patient was admitted to the medical service with a diagnosis of exophthalmic goiter and chronic myocarditis.

Treatment and Course—The patient was considered a poor operative risk, and treatment consisted of rest in bed and a high caloric diet. He did not improve during ten weeks of this treatment. On May 16, the basal metabolic rate was 67 per cent, and the average pulse rate, 110. On this date 10 cc of absolute

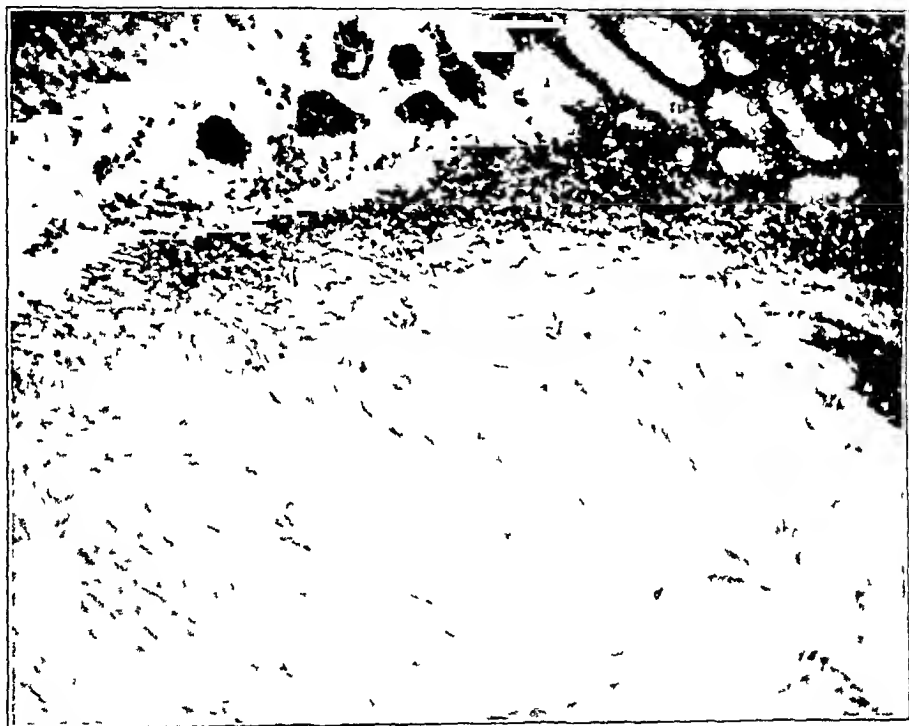


Fig. 8 (case 7)—Border of dense scar tissue around another large area of necrosis connected with necrotic adenoma, advanced encapsulation.

alcohol was injected into each lobe of the thyroid. A moderately severe general reaction followed but subsided after three days. The patient was discharged, he weighed 104 pounds (47.2 Kg).

On September 16 he returned to the hospital weighing 125 pounds (56.7 Kg) and showing much symptomatic improvement. The basal metabolic rate was 50 per cent and the average pulse rate was 94. On this date, 14 cc of absolute alcohol was injected into each lobe of the thyroid. There was a slight reaction, and he was discharged from the hospital on September 17.

On October 20, he returned. He weighed 127 pounds (57.6 Kg) and was much less nervous. The basal metabolic rate was 47 per cent and his average pulse rate was 90. On October 22 12 cc of absolute alcohol was injected into each lobe and was followed by little reaction. He left for home the following day.

He returned on December 11 when his general condition was about the same. The basal metabolic rate was 50 per cent, his weight was 143 pounds (65 Kg) and the pulse rate averaged 90. On Jan 15, 1925, he was in about the same general condition, but the operative risk was thought to be good and a subtotal thyroidectomy was done. Convalescence was uneventful. The specimen removed showed "epithelial hypertrophy, hyperplastic rudimentary lymph nodes with large areas of necrosis."

In July, 1926, he reported that he was in excellent condition.

CASE 9—History—Miss J. Mc., aged 34, a stenographer, came to the hospital on May 28, 1924, complaining of weakness and nervousness. A sister had had exophthalmic goiter. The present illness began in February, 1924 with nervousness and enlargement of the neck. In April, she began to have palpitation and dyspnea on exertion. Her best weight was 124 pounds (56.2 Kg) in October 1923, and she weighed 105 pounds (47.6 Kg) at the time of entrance. Her appetite was voracious, and diarrhea and vomiting had not occurred.

Examination—She was undernourished and nervous. There was a moderate grade of exophthalmos. The thyroid gland was symmetrically enlarged without a thrill or bruit. The lungs were normal, the heart was slightly enlarged and overactive. The blood pressure was systolic, 130, diastolic 68. The abdomen was normal. The extremities were normal, except for a tremor of the fingers. Laboratory examination showed normal urine, a negative blood Wassermann reaction and slight secondary anemia. An electrocardiogram showed sinus tachycardia. The basal metabolic rate was 62 per cent.

Treatment and Course—She was placed in bed on a high caloric diet. She improved somewhat, and on June 10, the basal metabolic rate was 43 per cent and the pulse rate, 100. On June 25, the basal metabolic rate was 49 per cent. She had continued to lose weight, until at this time she weighed 99 pounds (45 Kg). On June 26, 10 cc of absolute alcohol was injected into each lobe of the thyroid. There was a moderate reaction and she was discharged on July 1.

On July 17, the patient reported by letter that she was improving. On August 30, she wrote that she felt well and had been working several hours a day, against our advice.

On September 10, she returned. Her weight was 104 pounds (47.2 Kg), and the basal metabolic rate, 35 per cent. Ten cubic centimeters of absolute alcohol was injected into each lobe. There was little reaction and she was discharged two days later.

On October 15 her weight was 108 pounds (49 Kg), the basal metabolic rate was 38 per cent and the average pulse rate was 100. Fifteen cubic centimeters of absolute alcohol was injected into the right lobe and 10 cc into the left lobe. She returned home the following day.

On November 19, her weight was 112 pounds (50.8 Kg), the basal metabolic rate, 25 per cent, and the average pulse rate, 90. Symptomatically she was much improved. On December 20 her weight was 120 pounds (54.4 Kg), the basal metabolic rate, 27 per cent and the average pulse rate 90.

At this time a subtotal thyroidectomy was done without bad results, and her convalescence was without event. The specimen showed "epithelial hyperplasia and hypertrophy. Hyperplasia of the rudimentary lymph nodes. Large areas of necrosis with beginning organization."

In January 1927 the patient reported that she was in good condition.

CASE 10—History—Mrs. L. R., aged 52, a housewife entered the hospital Jan 23 1924 complaining of weakness, loss of weight and exophthalmos.

Twenty years before she had had an illness accompanied by a rapid pulse loss of weight and marked nervousness. During this attack, her eyes had become prominent. After spending seven months in bed, she had improved, and while she had not been entirely well she had carried on her usual duties. In November, 1923, she had again become nervous and the exophthalmos had become more marked. Her weight was reduced from 128 to 108 pounds (58 to 49 Kg.).

Examination—She was nervous and emaciated. Extreme exophthalmos was noted. The thyroid was slightly enlarged and very firm. Definite thrill and bruit were observed. The lungs were normal. The heart was moderately enlarged and overactive, and the pulse rate was 130. A blowing systolic murmur was loudest over the mitral area. The blood pressure was 138 systolic and 68 diastolic. The abdomen was normal. The extremities were normal except for tremor of the fingers.

Laboratory Observations—The urine was normal. An electrocardiogram showed sinus tachycardia. The basal metabolic rate was 76 per cent.

The diagnosis was acute exacerbation of a chronic type of exophthalmic goiter.

Illness and Course—She was placed in bed, and given sedatives and a high caloric diet.

On February 10, she had not improved, and the superior thyroid vessels on both sides were ligated. This was followed by a moderately severe reaction. A few days later, she was sent home.

She returned on April 10, without symptomatic improvement. Her weight was 100 pounds (45.4 Kg.), and the basal metabolic rate was 70 per cent. On April 12, 10 cc. of absolute alcohol was injected into each lobe. There was a mild reaction, and she was discharged a week later.

On June 2, she returned, somewhat improved. Her weight was 105 pounds (47.6 Kg.), and the basal metabolic rate was 54 per cent. Ten cubic centimeters of absolute alcohol was again introduced into each lobe, and she was sent home.

On July 12, she returned, showing further improvement. Her weight was 110 pounds (50 Kg.), and the basal metabolic rate was 45 per cent.

She was not seen again until 1925, when she stated that she had felt fairly well from August, 1924 until January, 1925, and had carried on her usual work. Since January, she had had a return of symptoms, she weighed 105 pounds (47.6 Kg.) and the basal metabolic rate was 65 per cent. The right lobe was removed, and a sharp reaction followed. She went home with instructions to return but she did not do so until Feb. 23, 1926. There had been so much relief from the lobectomy that she had considered herself well until December, 1926 when the symptoms returned. The basal metabolic rate was 75 per cent and the weight 103 pounds (46.7 Kg.). The left lobe was removed, this was followed by a severe reaction. She was seen in January, 1927, and was in good condition. The basal metabolic rate was 12 per cent, and she weighed 120 pounds (54.4 Kg.).

COMMENT

Ten patients were treated by the foregoing method. Some of them had been under observation for as long as two years. In most cases the operative risk was considered poor at the onset of treatment. All except the patient in case 10 showed marked symptomatic improvement with gain in weight, decrease of nervousness and decrease of pulse rate. Some diminution of the basal metabolic rate was noted but this was not

remarkable in many of the cases. In seven cases the eventual improvement was sufficient to class the patients as good operative risks, and subtotal thyroidectomies were performed. Three patients improved so much after several injections that further treatment was not necessary. All of these patients rested in bed for long periods, under supervision, without marked improvement, while in some instances the symptoms actually increased in severity. The patients were selected from the group of patients who did not show sufficient improvement under recognized methods of treatment to allow lobectomy or subtotal thyroidectomy. Some of them had received roentgen-ray therapy, others had been treated by superior pole ligation, but in every case enough time had elapsed after these measures had been employed to determine the maximum improvement before the injection of alcohol was begun. With the present method of treating patients with severe hyperthyroidism, this procedure is not commonly needed, but we believe that it can be used advantageously in a small group of patients who do not respond to the usual preoperative treatment. Since the completion of these studies, approximately 1,600 patients with goiter have been treated surgically in this clinic. Of this group, fourteen patients were treated also with alcohol as a preoperative measure, with results similar to those here reported.

SUMMARY AND CONCLUSIONS

- 1 Absolute alcohol can be injected into the thyroid of patients with hyperthyroidism without harm to them.
- 2 The local histologic changes are similar to those found in the experimental animals: an initial coagulation necrosis, followed eventually by replacement of the thyroid tissue by fibrous tissue.
- 3 The procedure is without technical difficulties.
- 4 The local and general reactions are slight.
- 5 An improvement in the patient's condition can be produced depending on the amount of gland destroyed by the alcohol.
- 6 The procedure is not intended to replace subtotal thyroidectomy but is applicable in a small group of cases in which all other methods have failed to make the operative risk good.
- 7 Pseudoglandular adhesions result, which make the complete operation more difficult, but by the use of small amounts of the alcohol injected frequently this can be made a negligible factor.

THE INTERNAL CALLUS

AN EXPERIMENTAL STUDY

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SAN FRANCISCO

The term "internal callus" is employed frequently by those who treat patients who have sustained fractures, this and other names are mentioned in textbooks. Blaisdell and Cowan described it in a series of experiments on kittens¹. The late Dr. Edward Hall Nichols conducted a series of experiments on animals to demonstrate the internal callus, which he showed to me shortly before his death but I believe they have never been published. The experiments I have conducted were prompted by those of Dr. Nichols.

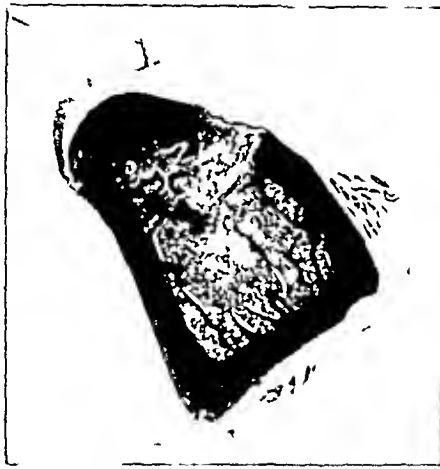


Fig. 1 (cat 42) — Cross-section of the tibia at the site of operation, showing the hole in the cortex plugged with bone and fibrous tissue.

In the roentgenograms showing healing fractures one sees little, if any, internal callus. It was absent in several series of experimental fractures of the humeri of cats, or was occasionally present in a rudimentary degree. In these fractures, of course, much deformity and overriding were unavoidably present, and all nature's effective efforts at healing were expended on the outside of the cortex beneath the periosteum. The internal callus is supposed to be more in evidence in frac-

*From the Stanford University Laboratory of Surgical Research.

1 Blaisdell, T. E. and Cowan, J. F. Healing of Simple Fracture. *Arch. Surg.* 12: 619 (March) 1926.

2 Ely, Leonard W. An Experimental Study of the Healing of Fractures. *Arch. Surg.* 5: 527 (Nov.) 1922.

tures with accurate apposition, this is possibly true, but is difficult to demonstrate, if the fracture is a complete one

The problem that interested me was the method of repair of an injury to the shaft of a long bone when there was no actual solution of continuity, and therefore no necessity for nature to build a wiped joint, so-called, under the periosteum—the method she employs when the shaft is completely fractured. I selected cats for the experiment, cut down on the anteromedial aspect of the shaft of the right tibia, incised the peri-



Fig. 2 (cat 36) —Note the bridge of fibrous tissue at the surface, the incomplete bridge of bone trabeculae farther in, the new bone trabeculae along the cut surfaces of the cortex and the scattered trabeculae in the marrow canal

osteum, and with a small drill bored a hole about 2.7 mm in diameter into the marrow canal. Then I closed the wound and applied a collodion dressing. All operations were performed under complete ether narcosis and with strict asepsis. The cats died or were killed at various intervals. The bone was removed, fixed in 10 per cent formaldehyde, decalcified in 5 per cent nitric acid, run through the alcohols and ether and mounted

in celloidin. I operated on eleven cats but in six of them the wounded area could not be identified. The results in the other five are given in detail. There were no infections of the bone.

PROTOCOLS

CAT 36—This cat was examined sixty-seven days after operation. The hole in the cortex was plugged with fibrous tissue, which was continuous with the periosteum, and streamed down in a long band through the marrow canal almost



Fig 3 (cat 40) — The illustration shows the new trabeculae at the side of the hole, on the outside of the cortex, and the incomplete bridge of new trabeculae across the hole near the surface, with fibrous tissue and scattered bone trabeculae deeper in. A second incomplete bridge of new bone trabeculae has formed in the marrow canal below the level of the cortex.

to the opposite cortex. In it, as it passed through the hole in the cortex, several larger and smaller areas of bone had formed. Bone trabeculae had also formed at the sides of the hole on the cut ends of the cortex and this new liver of bone was continuous with one of considerable thickness on the outside of the cortex under the periosteum and also with another much thinner, on the inside of the cortex. There was no suggestion of bridging of bone across the gap at the surface.

CAT 40—This cat was examined thirteen days after operation. Near the surface, between the cut margins of the cortex there was an irregular mass of fibrous tissue across the gap, continuous with the periosteum, and this fibrous tissue extended irregularly down into the hole. In its superficial portion, almost at the outside level of the cortex, a bridge of new trabeculae was forming. Deeper in the hole numerous trabeculae were building up, apparently from the fibrous tissue, just below the level of the inner cortex these trabeculae were much thicker and had formed an almost complete bridge across the gap. At a short distance below them, well out in the marrow cavity, another new island of bone

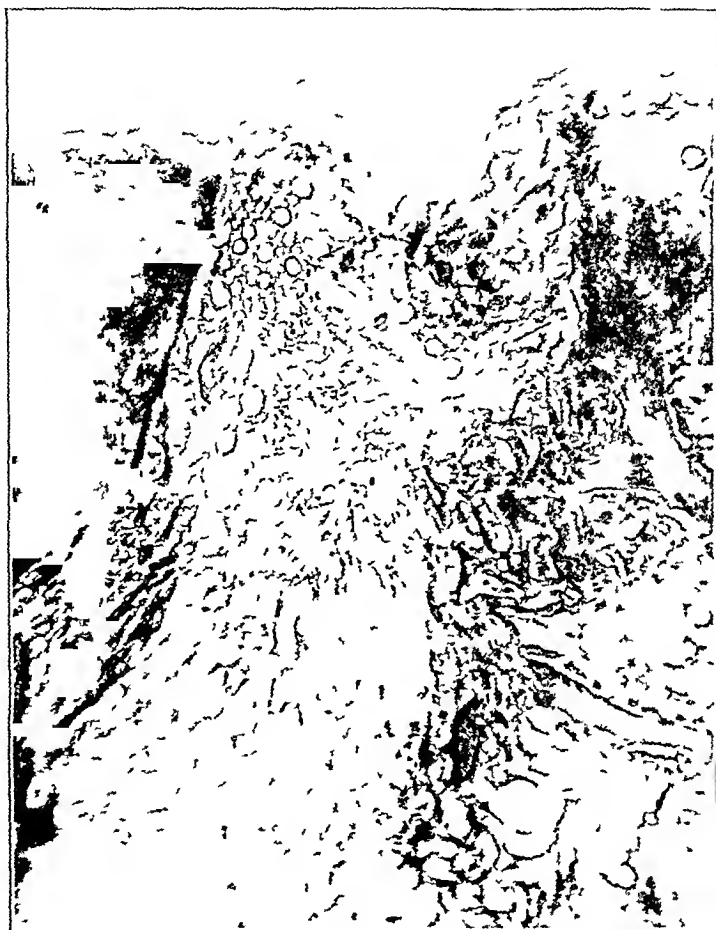


Fig 4 (cat 41) —New bone trabeculae on the outside of the cortex. The hole is plugged with fibrous tissue with scattered bone trabeculae. Many new trabeculae have formed beneath the level of the cortex, but the ones in this particular slide do not show much bridging across.

was developing in fibrous tissue. Scarcely any bone was developing on either of the cut surfaces seen in the slide. At one side of the gap new trabeculae were developing on the outside of the cortex, but these did not appear on the other side.

CAT 41—This cat was examined fourteen days after operation. The soft parts of the bone had been removed over the hole in the preparation of the specimen, so that the question of the continuity of the periosteum could not be determined. A marked proliferation of bone had taken place on the outside of the cortex for

some distance on each side of the hole, as usual it was thicker in the immediate vicinity of the hole, and tapered off as the distance from the hole increased. Many trabeculae were seen in the fibrous marrow beneath the level of the cortex, and these formed an incomplete bridge across the hole below the level of the cortex, in the fibrous marrow. Evidence of any new formation of bone on the cut margins of the cortex could not be seen. The inner aspect of the cortex near the hole also showed some new bone trabeculae.

CAT 42—This cat was examined thirty-four days after operation. When the skin was removed from the leg of the animal after death a distinct soft mass



Fig. 5 (cat 42)—The hole has been bridged across at the surface by fibrous tissue and in the deeper portion of this fibrous tissue an incomplete bridge of new bone trabeculae has formed, continuous with the new bone layer formed on the cut margins of the cortex. Scattered trabeculae can be seen deeper in the cut and many also below the opening, in the marrow canal.

appeared under the deep fascia at the site of the wound. This had the appearance of the ordinary cheesy material occasionally found after operations on animals whose wounds are infected, but there was no other sign of infection.

The periosteum passed across the hole and continued through its center as a rather thin strip of fibrous tissue which extended into the marrow canal. Bone trabeculae were forming in the bone in this fibrous strip. A thin strip of bone had been laid down on each side of the cut surfaces of the bone and this was

continuous with the new trabeculae formed in the hole. Trabeculae were especially noticeable just beneath the periosteum, but many had formed beneath in the marrow canal. Distinct evidence of external callus could not be seen.

CAT 43—This cat was examined forty-two days after operation. The periosteum stretched across the hole, and directly beneath this, in the fibrous tissue, an almost complete bridge of bone trabeculae had developed. New bone had also formed on the cut surface on each cortical margin. A few trabeculae were scattered in the cellular marrow which occupied the rest of the hole. The blood sinuses were distended with blood cells. A few other trabeculae were present



Fig. 6 (cat 43)—Note the strip of fibrous tissue across the hole at the surface with the almost complete bridge of bone beneath it. Deeper, scattered trabeculae can be seen.

in the marrow beneath the hole, but these were not as numerous as in some of the other specimens. No new formation of bone was present on the outside of the cortex.

SUMMARY

When a hole is bored into the cortex of a long bone of an animal it becomes filled with fibrous tissue which is continuous with the periosteum and often extends well down into the marrow canal. Instead of forming a barrier to bony union, this formation of fibrous tissue is evidently a

step in the healing process. In it bone trabecule form irregularly. Sometimes they are most numerous near the surface of the cortex, sometimes in the hole and occasionally in the marrow beneath the hole. Often new bone is formed on the outside of the cortex, but this seems to play little if any rôle in the filling up of the hole. It may be absent. I have not observed any necrosis of the cut margins of the cortex as described in many textbooks. Contrary to what I had believed before, bone is actually produced on the cut margin of the cortex. Cartilage was absent in the healing process.

CEREBROSPINAL FLUID

NORMAL VARIATIONS IN THE RATE OF FORMATION¹

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During the routine care of neurosurgical patients with obstructive hydrocephalus, periodic drainage of the ventricles has been necessary for the relief from intracranial pressure in a number of cases. It has been noted repeatedly that in the early morning the symptoms of pressure develop much more slowly, and, furthermore, that after longer periods of time, drainage of the ventricles yields less fluid than at other times during the day. This has been observed so constantly that at present it is customary to allow these patients to go from midnight until 8 or 9 a. m. without drainage. Even then the intracranial pressure and the quantity of fluid obtained is less than after a four to six hour interval during the later part of the morning or evening.

The most striking illustration of this diurnal and nocturnal variation in the formation of ventricular fluid was given by a patient in whom continuous drainage of the cisterna magna and ventricles was established because of obstruction about the base of the brain (case 1). Figure 1 shows an almost total absence of drainage in the hours immediately after midnight, while there is a noticeable decrease in the amount of fluid in the early afternoon. On the other hand, the largest amount of fluid was obtained in the morning and evening hours from 7 or 8 to 12 o'clock.

In the only other case of continuous drainage of the ventricles, a tube was inserted into the enlarged ventricle through the occipital region. An accurate hourly record of the amount of fluid was not obtained, however, the nurse's notes covering several days report "no drainage in the early morning and toward daybreak" "tube draining well." In the latter case there was no manipulation of the tube at any time, in the former case, with the hourly record shown in figure 1 every night when the drainage stopped the tube was disconnected, warm Ringer's solution was run through it and fluid aspirated, at times the ventricles were tapped. Blockage of the drainage tube was not found and there was no increase in the intraventricular pressure. Several hours later the drainage would begin spontaneously without further adjustment of the tube.

This variation was so striking that the records of several patients in whom periodic drainage had been instituted were studied. The fluid

¹ From the Surgical Department of the Johns Hopkins University and Hospital.

obtained had been accurately measured and recorded together with the time of the ventricular puncture. This method of drainage is easy and reliable as there is no question of the patency of a tube. Each time the ventricles were drained until all pressure was relieved. Figures 2, 3, 4, 5 and 6 are sections of the charts which were made, all of them showing that in the early morning much less fluid is formed than at other times.

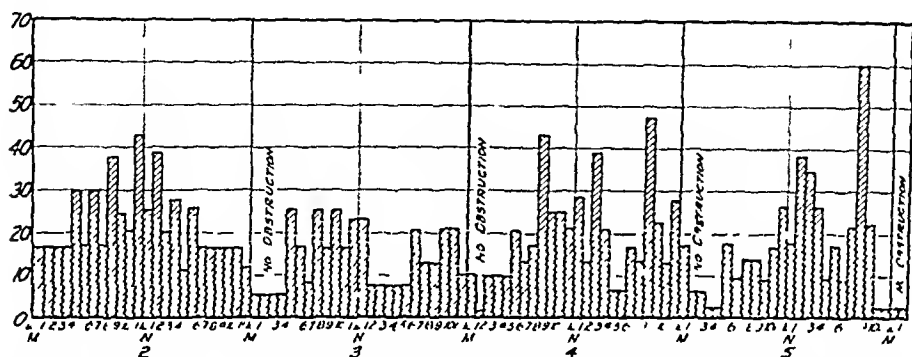


Fig 1 (case 1) —The hourly record of the drainage of cerebrospinal fluid in a patient having a block about the base of the brain. The chart begins at midnight of the day of operation so the relatively larger amount of drainage for the first few hours might be explained partly as being serum and partly as a response to the irritation of this foreign substance. The decrease in the amount of drainage for the early morning and afternoon hours is evident. No obstruction indicates the points at which the drainage tube was tested and found to be patent.

In this and the subsequent charts the amount of fluid is indicated in cubic centimeters on the side. The hours are recorded beneath, while midnight is indicated by a double vertical line and *M* at the base, noon by a single vertical line and *N* at the base. Beneath the *N* is given the postoperative day.

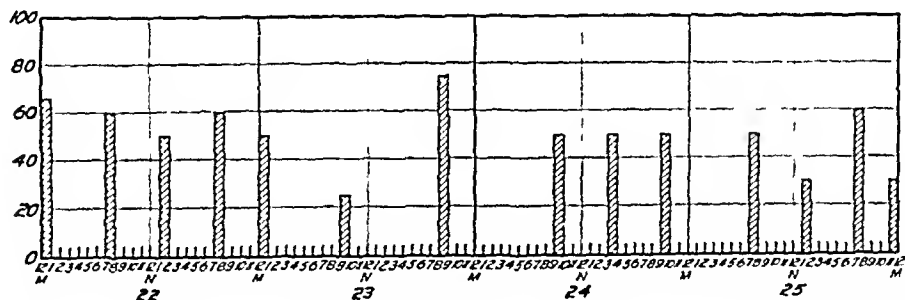


Fig 2 (case 1) —The periodic drainage of the ventricles for the twenty-second to the twenty-fifth postoperative days. In this and the subsequent charts the hour of the ventricular puncture is recorded at the base, and the amount of fluid (indicated in cubic centimeters at the side) is given by the height of the column. If the time interval between punctures is considered, it is seen that the least amount of fluid is formed during the early morning hours.

during the day. This is particularly well demonstrated when the ventricular punctures were made around 4 or 5 a. m. (fig 3) but if the interval of time is considered it is seen that this is uniformly true. Of course punctures performed after 8 or 9 a. m. should be discounted since

the time interval includes part of the period of more profuse drainage or formation of fluid

A pronounced demonstration of this decreased formation of fluid in the early morning was given by a patient, aged 30 who had a bilateral hydrocephalus caused by a metastatic melanotic sarcoma just over the aqueduct of Sylvius (fig 7). Every four to six hours during the day he would become progressively drowsy and finally comatose. When the intracranial pressure was relieved by a ventricular tap he would rouse

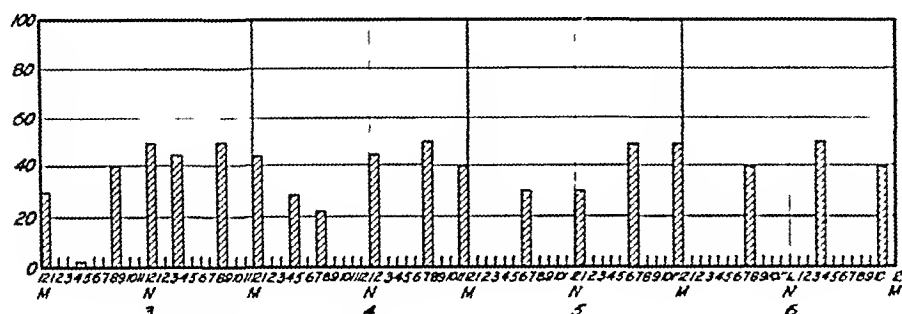


Fig 3 (case 2) —This chart also shows the decreased amount of fluid in the early morning hours. This is particularly well illustrated on the third and fourth days after operation, when the ventricles were drained between 4 and 5 a. m. and little fluid obtained. The patient drank large quantities of fluids and each night between 12 and 8 a. m. would take from about one third to one fourth of the total fluid intake for the twenty-four hours.

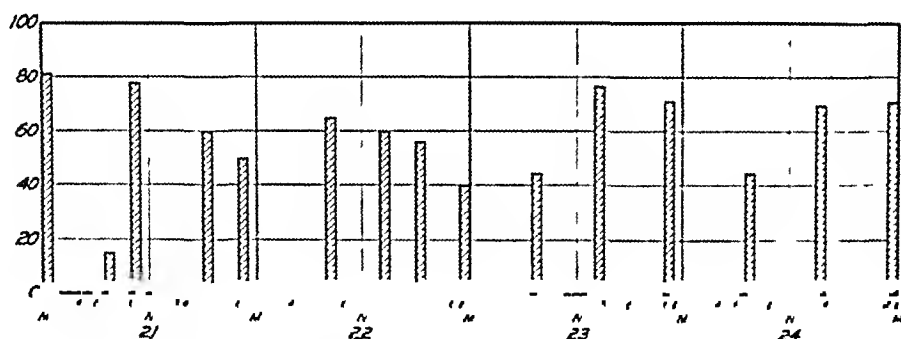


Fig 4 (case 3) —The periodic drainage of the ventricles in a case of hydrocephalus with a tumor removed from the region of the pineal and third ventricle. The decreased amount of ventricular fluid in the early morning hours is striking; this occurred in a patient who was drowsy, who gave no apparent thought to his surroundings and who was receiving fluids by gavage by subpectoral intubation and by rectum. Accordingly there was little variation in the amount of fluid taken during a given interval of time regardless of whether it was night or day.

and ask for water or food while the fluid was still draining from the needle. He would remain bright for from one to three hours afterward, but it was always necessary to relieve the pressure just before meals were served. However, after from six to nine hours had elapsed at night without ventricular drainage, he would awake in the morning

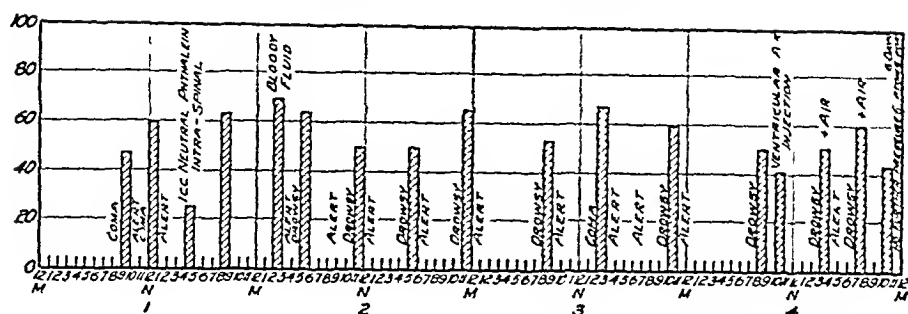


Fig 5 (case 4) — Besides the variation in the amount of ventricular fluid formed during the day and night, this chart shows the much larger quantity of fluid obtained after intraspinal injection of neutral phthalein and when bloody fluid was present within the ventricles. This reaction, probably mostly due to the presence of the blood, passed away within twenty-four hours. Note also the reaction following the ventricular injection of air with more rapid development of intracranial pressure, the larger volume of air and fluid released from the ventricles and the spontaneous relief from all pressure symptoms for the six days following the injection. This relief was apparently the result of the forcing open of the aqueduct which was closed by a small overlying tumor (fig 7). The word 'drowsy' was used on the chart regardless of whether the patient was drowsy or comatose. In general, the state of consciousness corresponded inversely to the amount of fluid within the ventricles. It was most notable that after a longer period of time at night the patient would waken and eat breakfast before the ventricles were drained, whereas during the day they had to be tapped before each meal.

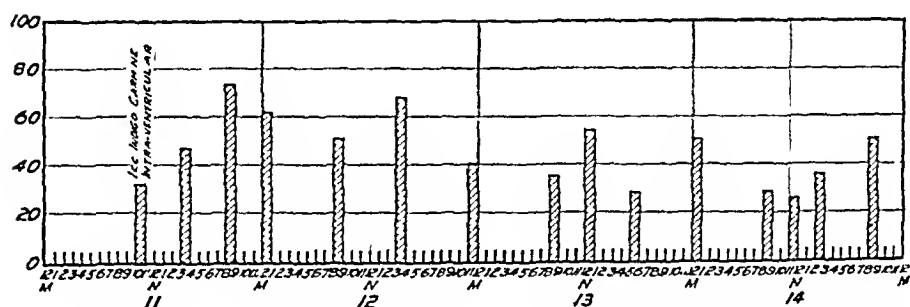


Fig 6 (case 4) — A continuation of the same case as that represented in figure 5 after the six days of relief from symptoms of increased intracranial pressure. It shows in addition to the variation in the quantity of ventricular fluid from the day to night that there was a considerable increase in the total amount of fluid obtained for the twenty-four hours after the intraventricular injection of indigo carmine. This dye did not pass through to the spinal fluid indicating a complete block which later at autopsy proved to be at the aqueduct (fig 7).

cooperate in being prepared for the day, and frequently eat his breakfast before becoming comatose. The punctures made in the morning after this longer period of time were always productive of less fluid than those made during the day, and the patient was never in coma (figs 5 and 6). Figure 3 is even more striking, showing the results of two punctures performed between 4 and 5 a m., little fluid being obtained.

There are certain exceptions to this rule of diminution in the amount of drainage during the early morning and afternoon, these cases come under the general classification of some irritating substance within the ventricles. Figures 5 and 6 show the results of injection of air and neutral indigo carmine into the ventricles in such cases. Neutral phenol-sulphonphthalein was also injected into the spinal canal (fig 5) causing



Fig 7 (case 4)—A cross-section of the brain of patient J. McC. (figs 5 and 6) with a nodule of metastatic melanotic sarcoma just above the aqueduct. The aqueduct is compressed to a slit, and the temporary opening of this could explain the relief from intracranial pressure following the injection of air (fig 5).

a marked increase in the amount of ventricular drainage for the following twenty-four hours. This was true when there was a complete block at the aqueduct, as was proved by the fact that the dye did not come through to the ventricles. This could possibly be explained by the secondary pressure exerted on the ventricles by either the extravasation of fluid or the lack of absorption of fluid in the subarachnoid space as a result of the irritating action of the phenolsulphonphthalein. It seems more likely, however, that the blood in the ventricular fluid as noted in figure 5 was more probably the irritating factor, since it was within the ventricle. Careful study of the record of the case of another patient who failed to show this marked decrease in the amount of fluid at night revealed that he had an intraventricular tumor and bloody ventricular

fluid was frequently noted. It has been frequently observed that in neutral phthalein, neutral indigo carmine or blood within the ventricles act as irritants, and their presence demands more frequent tapplings for relief from intracranial pressure, this more rapid formation of fluid does not follow the general curve shown in figure 1. The greater part of this irritating action has usually passed away within twenty-four hours.

The irritation from air seems to last longer and be more pronounced than that caused by either the neutral phthalein or by indigo carmine. This is particularly true in the presence of obstructive hydrocephalus. An unexpected exception to this observation was the injection of air as shown in figure 5. Apparently the increased pressure as a result of the irritation of the air forced open the aqueduct and allowed the fluid to reach the subarachnoid space, where it was absorbed (fig. 7). The patient was relieved from symptoms of pressure for six days after the injection, and the actual record of intracranial pressure by ventricular puncture showed that there was no elevation. This can be readily understood by a glance at figure 7, which shows the small metastatic melanotic tumor just over the aqueduct, where it could readily cause temporary blockage to the passage of fluid from the third ventricle.

In all of the patients studied to obtain data for the charts and particularly in the patients in the first four cases which are reported, the presence of a block was determined or proved by one or more of the following methods: (1) by the injection of neutral phthalein, indigo carmine or air, (2) by ascertaining the presence of a bilateral hydrocephalus accompanied by a difference in the color and character of the ventricular and spinal fluid (i.e., amount of blood globulin, etc.) and (3) by operation or postmortem examination.

In addition, the intracranial pressure would lead one to suspect that a block was present or that there was a marked diminution in the amount of fluid absorbed. When there is complete blocking off of the ventricular system from the subarachnoid space the amount of fluid that can be absorbed is minimal and can be ignored. The amount of fluid obtained by drainage is as near the total amount formed as it is possible to obtain by experimental methods. It seems proved, therefore, that there is a definite and marked variation in the amount of ventricular fluid which is normally formed during different periods of the day and night.

I have no proved explanation of this variation to offer. Every nurse's chart was gone over carefully. The temperature and the pulse and respiration rates did not show any change other than the usual response to increased intracranial pressure.

No correlation could be determined as to the intake and output of fluid. Some of the patients were given nasal feedings late at night, others received the major portion of their fluids by subpectoral infusion.

and dextrose by rectum both day and night without variation. The record of one of the patients who was able to take fluid by mouth showed that over a period of eight days there was only one night during which the fluid intake, between midnight and 8 a. m., was less than from one third to one fourth of the total amount taken during the twenty-four hours (fig. 3). When the fluid intake is markedly insufficient causing body dehydration there may be a decrease in the amount of the ventricular fluid. An extreme example of this is the case of a man with obstructive hydrocephalus who was brought to the hospital in coma and who was having convulsions every five or eight minutes. Trephine openings had previously been made for diagnostic purposes. The ventricles were tapped, and the intracranial pressure was considerably less than the atmospheric pressure. He was immediately given 800 cc of 5 per cent dextrose intravenously and a subpectoral infusion of salt and the administration of 5 per cent dextrose by rectum was started and allowed to run slowly. The convulsions ceased within an hour and a half, a few hours thereafter the ventricles were tapped, and the fluid was found to be under markedly increased pressure. The convulsions did not recur during the remainder of the patient's stay in the hospital.

The only stimulants which had been given to any of the patients were coffee, tea, cocoa, coca cola and cigarets. These showed no demonstrable effect on the amount of drainage.

No relationship could be determined between the state of consciousness and the amount of ventricular fluid. At one time the patient was asleep and at another awake during the periods of decreased drainage. The little girl who would take a third of the total fluid intake for the day between midnight and 8 a. m., and who was frequently asking for water, was awake a great part of the time (fig. 3). It must be kept in mind of course, that even if the patient was awake, at this time of night there was far less outside stimulation in the form of noises, light and general activity than during the day or evening. This, however, would not explain the less definite drop in the afternoon. Some patients who were always in a stupor showed this variation. The only definite relation between consciousness and the amount of fluid was the drowsiness and stupor secondary to pressure, and these were more pronounced and came on more rapidly during the day or early evening. Headaches and vomiting were sometimes associated with these symptoms. The headaches, however, were as severe when there was a complete reduction of pressure as when there was too much pressure.

It might be thought that the movements of the body would influence the amount of fluid where there was continuous drainage. A careful record of any changes in position, however, fails to show any increase or decrease in the amount of fluid following either voluntary or passive turning.

On looking back over these cases it seems highly probable that there was a parallel between the blood pressure and the amount of ventricular fluid, but since no simultaneous record was kept, this cannot be proved.

Many possibilities of investigation are suggested. For instance the following points might be studied: (1) the relation of blood pressure to the amount of ventricular fluid, (2) the relationship of fluid intake and output to intracranial pressure and the formation of ventricular fluid particularly with reference to low fluid intake, (3) the influence of drugs and stimulation on the amount of fluid and (4) whether or not at any particular time drugs in the blood stream are more apt to gain access to the ventricular fluid, etc.

SUMMARY

There is a marked variation in the formation of cerebrospinal fluid for the different periods of the day and night. In general there is a decrease in the amount of fluid in the early morning and afternoon and an increase in the forenoon and evening. The practical cessation in the formation of fluid for the few hours after midnight is most striking.

A considerable number of substances, in general classed as irritants (an, neutral phthalein, neutral indigo carmine, blood, etc.) in the ventricles will give a marked increase in the formation of fluid without regard to the time of day or night, and demand more frequent tapping for relief from pressure.

There is no proved explanation as to why this occurs but it seems probable that it is related to general vital activities. Possibly it parallels the blood pressure curve. There may be some similarity to the variations in the amount of urinary secretion, but this is not so striking as to show that it is directly influenced by the fluid intake.

REPORT OF CASES

CASE 1—History—(History obtained from the patient's father, a physician) W. M. aged 16 complained of disturbance of vision and gait, and projectile vomiting. The onset of the present illness was dated from a fall for a distance of about 4 feet and 2 inches (127 cm.) at the age of 14 months when the child struck his head. He was unconscious for a few minutes and had a laceration of the head which healed by granulations. Following the injury the patient had a bilateral paralysis which lasted for three weeks but after six weeks he was thought to be normal. During this time he had attacks of vomiting and cried a great deal. (In later life these attacks of vomiting persisted and then the patient complained of associated headaches.) When the patient was about 30 months of age it was noted that there was a paralysis of the extra-ocular muscles on the left side. This cleared up after six months but after that time there was some weakness of the external recti on both sides.

There was no particular trouble until the patient was 6 years of age when he was thrown from a horse and was unconscious for an hour. For the two days following he was unable to stand. He had always been clumsy and the clumsiness increased after this fall. At 8 and also at 12 years of age the patient

had falls which were severe and which were caused by his clumsiness. When 12 years old, he tripped while running and struck his head. Severe headaches followed for twelve days. He fell again and was found on the lawn turning around and around, always toward the right and complaining of his head. After a short time he fell unconscious. The following day he was unable to walk and remained in bed in a hospital for sixty-one days, with a temperature ranging from 100 to 102.5 F. He was drowsy most of the time and complained much of headache. For the following sixteen days he could walk with support and then was able to get about alone. His condition was then fairly satisfactory for two years. About two years before presentation, at the age of 14 the headaches again came on and became more constant and more severe. Since then it had been noted that he staggered toward the right. The disturbance of gait and the awkwardness and clumsiness became progressively worse.

In February, 1925, five months prior to presentation, following a cold he became much worse, almost over night. He was unable to walk and fell to the right. He had headaches and projectile vomiting, these symptoms grew progressively worse.

Examination—The patient was a rather obese white boy, aged 16, who showed no evidence of outdoor life. He had a very large head, and wore a 7½ hat (hydrocephalus). The cranial nerves showed that there was marked impairment of vision in both eyes, and he was just able to count fingers. There was slight choking of the disks on both sides, more marked on the right. There was a paralysis of the external rectus muscle on the left and marked nystagmus on looking to either side. The pupils were large and reacted to light. Apparently sensation was normal on both sides of the face, but the corneal reflex was probably a little less acute on the right. A definite facial weakness was present on the right side. Some impairment of hearing was noted on both sides, air conduction being better than bone conduction. Other cranial nerves functioned normally.

Mentally, there seemed to be considerable impairment. There was weakness of the entire right side of the body, though it was thought that this might be due to a cerebellar lesion. Aphasia, hemianopia or uncinate attacks were not noted.

There was a markedly positive Romberg sign, the patient falling to the right. Ataxia was more marked on the right, both in the arms and legs, nystagmus was present. Adiadokokinesis was more marked on the right. The reflexes were normal.

First Operation—June 19, 1925. A cerebellar exploration was performed and a large, thrombosed hemangioma was revealed, the tumor was thought to be inoperable. The wound was closed. The patient made an uneventful recovery.

Second Operation—June 30, 1925. Cerebellar approach, second stage, was the procedure used this time. The thrombosed hemangioma was partially excised. The temperature rose rapidly, by evening it had reached 106.5 F., at which time it was decided to establish continuous drainage of the cerebellar region for relief from pressure which recurred rapidly after ventricular puncture.

June 30. The cerebellar wound was explored and a drainage tube inserted. The patient continued to improve during the night and remained conscious. Drainage was good, and the temperature gradually fell.

July 1. Drainage was free, 320 cc. for fifteen hours after operation, the fluid intake was 5,000 cc. for twenty-four hours.

July 2. The condition of the patient improved. He took large amounts of fluid by mouth. There was not so much drainage in the early morning, the tube was not obstructed.

were inserted into each of the lateral ventricles, and the air was removed by gradually filling the ventricular system with warm Ringer's solution. On account of the edema resulting from the operation over the aqueduct, the ventricles were tapped every four hours for the release of pressure, and considerable quantities of fluid under pressure were obtained. This periodic drainage was kept up for several days, and after the immediate effects of the operation began to wear off, the punctures were performed less frequently and finally discontinued, the area of cerebellar decompression being watched for fulness as an indication for ventricular drainage.

The patient was discharged twenty-five days after the last operation, able to walk. The eyes showed optic atrophy and marked impairment of vision. She was able to distinguish objects to which there was some contrast, and she was relieved from all symptoms of intracranial pressure. The cerebellar decompression was soft.

CASE 3—History—(History obtained from father) W. M., aged 12, dated the onset of the present illness to one year before presentation when he began to have headaches. Six months previously he began to have short attacks of dizziness associated with headaches and nausea. The headaches and vomiting continued with some remissions. One month previously, he became progressively weak and was unable to walk. There was a loss of control of the sphincter. There had not been any noticeable disturbance of vision nor any disturbance of swallowing, but recently, there had been progressively increasing difficulty in speech.

Examination—The patient was stuporous and did not move, to any question, after about a minute, he would answer "What?" There was weakness of the left internal rectus muscle, choked disk and tortuosity of the vessels on both sides. Facial weakness was noted on the right. Swallowing was apparently normal. Spasticity of the right arm and leg was noted, and sensation was apparently better on the right side. The patient was unable to sit up. The Babinski sign was positive on the right side and questionable on the left. Deep reflexes were hyperactive on the right. The diagnosis was probable cerebellar tumor.

Operation—June 22, 1926. Trephining and ventricular estimation were performed. After the injection of the indigo carmine, the color did not appear in the opposite ventricle until the fourth aspiration, and then faintly. Both ventricles were dilated tremendously. Even after the twentieth aspiration back and forth the fluid obtained from the right ventricle was much less colored than that on the left, where the dye was injected. On account of this discrepancy, a ventricular injection of air was performed.

One hundred cubic centimeters of fluid was aspirated from the left ventricle and the fluid replaced by air up to 65 cc. The usual series of roentgenograms were taken. These showed marked dilatation of the lateral ventricles and the third ventricle not filled. The air crossed the midline readily. The usual cerebellar exploration was made with cross-bow incision. There was fluid over the surface of the cerebellum and a small cisterna magna, herniation of the cerebellar tonsils had not occurred. The two cerebellar lobes were the same size, and their appearance was normal. Exploration of the cerebellopontile angle on either side and also of the fourth ventricle did not show any evidence of tumor. The floor of the fourth ventricle was scaphoid, so it was thought that there could not be a tumor of the underlying tissue of the brain. The pineal shadow suggested that there must be a tumor in that region, and accordingly the wound was closed. The patient made a fairly rapid recovery. Several ventricular punctures were

made each day to keep down the intracranial pressure. Thirteen days after operation, the patient vomited, he did this on several of the following days. This condition, as well as the state of consciousness, was improved by frequent ventricular tapplings. Improvement soon ceased, and several ventricular punctures a day were required for the relief from pressure, cultures of the ventricular fluid were negative for organisms, and twenty days after operation the patient was thought to be in condition for a craniotomy for exploration of the pineal region.

Second Operation—July 16, 1926. Right craniotomy was performed for pineal approach. A tumor in the pineal region and extending into the third ventricle was removed.

With the patient in the cerebellar position, a small flap was turned down, well posteriorly, the veins leading into the sinus were doubly ligated and divided, allowing the right cortex to fall away from the midline. The corpus callosum was exposed and divided for about 4 cm. The vein of Galen was ligated doubly and divided. The tumor was then dissected free, and all bleeding was controlled. The tumor was definitely circumscribed and projected into the third ventricle. After removal of the tumor, the operator could see most of the third ventricle.

The patient made a slow recovery, and frequent tapplings were necessary for relief from pressure. For ten days following the operation he continued to have a temperature as high as 103 F, but without evidence of infection in the ventricular fluid.

Third Operation—July 27, 1926. Trephining was performed for ventricular puncture because of local irritation about the trephine openings which had been in almost continuous use for over a month, and it was feared there would soon be danger of the infection being carried into the ventricles.

The patient lived for fourteen days following the last operation. At first he did not improve, and then he became progressively worse and more stuporous. The chest became more filled with mucus, the temperature rose and the pulse rate became rapid. Cultures of the ventricular fluid were negative up to the time of death. Autopsy revealed the aqueduct plugged with blood clot.

CASE 4—History—(History obtained from wife and father, a physician.) W. M., aged 31, complained of headaches and disturbance of vision. The present illness dated to two months before admission, when he began to have headaches and diplopia and to vomit. There were several operations on, and irrigations of the air sinuses about the nose. It was thought that there was some improvement for a short time. His condition became worse, and was accompanied by dizziness, choked disk, headaches and vomiting. A staggering gait was noted, and there was some occipital soreness. At times it had been difficult to arouse him. Otherwise his history was negative.

Examination—The results of the neurologic examination were negative except that considerable impairment of vision was found without restriction of the visual fields, marked choking of the optic disks, old and recent hemorrhages in the cerebra, with enlargement and tortuosity of the vessels. There was slight weakness of the superior rectus muscle on the left, and also some weakness of the external rectus muscle on this side. There was no nystagmus, but the patient was unsteady on his feet, and his gait was staggering. The impression was that there was a tumor of the brain of undetermined location.

Operation—Nov. 27, 1925. Trephining and ventricular estimation were performed. The usual occipital trephine openings were made, both ventricles were tapped and found to be dilated, with the fluid under increased pressure. One cubic centimeter of neutral indigo carmine was injected and passed rapidly over

to the opposite side, indicating that there was a block posterior to the third ventricle

A cerebellar exploration was made, but a tumor was not located. The patient made an uneventful recovery from anesthesia. The temperature rose to 103°. Ventricular punctures were performed about once a day, but only a moderate increase occurred in the pressure. The patient remained conscious and recognized his family.

December 6. There had been a marked change in the patient's condition within the past two days. He frequently became drowsy but was relieved by ventricular punctures, large quantities of fluid being withdrawn, and under fairly high pressure. At times it was necessary to drain the ventricles as often as every three or four hours. He received immediate relief from pressure with the drainage of the ventricles. He voided voluntarily, and ate fairly well. The respiratory rate was slow at times in accordance with the pressure. Lumbar puncture was performed with the injection of 1 cc of neutral phthalein in the lumbar spinal canal. None came through to the ventricular fluid over a period of twenty-four hours. The fluid from the spinal canal was definitely yellow, probably as a result of the recent cerebellar operation, while the fluid from the ventricles was more bloody and was not yellow. The total amount of ventricular fluid obtained during the day was 148 cc.

December 7. The condition remained about the same. It was necessary to puncture the ventricles frequently, five times during twenty-four hours, and a total of 299 cc of ventricular fluid was withdrawn. This increased quantity was thought to be due either to the bloody fluid in the ventricles or possibly to the injections of phthalein, though this did not come through to the ventricles.

December 8. There was little change in the condition of the patient, the punctures were not so frequent, only three were performed, 180 cc of fluid being released. It was noticeable that the patient did not show evidence of pressure during the night, but that early in the morning after the secretion of the fluid became more rapid, there was a rise in the pressure. Immediately following the release of the fluid, the patient became talkative and more alert mentally. He voided continually at times. Puncture was not performed between 11 p. m. and 8:30 a. m., at the morning puncture there was only moderate pressure, and only 53 cc of fluid was obtained. The usual amount was from 60 to 75 cc for shorter periods of time. When the next puncture was performed at 1:30 p. m., after an interval of only five hours, the pressure was greater, and 68 cc of fluid was obtained.

December 9. Little change was noted in the condition, but it was again noticeable that the patient did not develop signs of pressure throughout the night. Ventricular puncture was not performed between 10:30 p. m. and 8 a. m., and the patient was just becoming drowsy when the fluid was drained. Only 50 cc was obtained.

It should be noted that whenever there was pressure there was a marked increase in the deafness, even if the patient was still able to talk. There was no diminution in the associated corneal reflex. The patient was sent to the operating room for ventricular injection of air, so that before the pineal region was explored it might be ascertained that there was no cortical tumor.

Second Operation—Dec 9, 1925. The right ventricle was tapped, and 100 cc of fluid was aspirated and replaced with 75 cc of air. The roentgenograms showed that the ventricular system was uniformly dilated throughout, including the third ventricle, and that no distortion was present. No air reached the subarachnoid space within half an hour following the injection.

The air was released from the ventricles on two occasions at short intervals and with considerable increase in the intraventricular pressure. Throughout the remainder of the day, the patient seemed brighter than before the injection of air. The ventricles were tapped on two occasions during the evening and it was expected that they would have to be tapped during the night.

December 10 The patient remained clear mentally, and did not show any symptoms of pressure. When the ventricles were tapped in the morning only 38 cc of fluid was obtained, and it was not under marked pressure. The patient was conscious, and was better than at any time during the preceding ten days. During the remainder of the day, he was bright and talkative and said that he could see better. The disturbance of the extra-ocular muscles was not so great and he seemed to be generally improved.

December 12 The patient continued to improve. Further punctures were not made. Headaches did not occur and the patient could hear better, which was determined by the audiometer. He did not like to be disturbed, however and lay quiet except when it was necessary for him to move.

December 15 The patient's condition had been growing progressively worse for the past three days. He was listless, and frequently would not respond though he was able to talk when he desired. The ventricle was tapped on the previous day, only 28 cc of fluid was obtained, and this was under moderate pressure. The left ventricle was tapped, and fluid was obtained under moderate pressure. One ampule of neutral indigo carmine was injected and four hours later a lumbar puncture was performed, but there was no evidence of dye in the fluid obtained. The ventricle was then punctured, the dye was obtained in concentrated form. The fluid was under more marked pressure, and there was a little rise in the temperature up to 101.5 F following the injection of the dye.

December 18 In order to obtain relief from the intracranial pressure, it was necessary to puncture the ventricles frequently after the injection of the indigo carmine.

It was learned that about a year previous to presentation the patient had had a pigmented tumor removed with radium from the sole of the left foot. This was done because the tumor had become ulcerated. There were some moderately enlarged lymph glands in the groin. One of these was to be excised on December 18, since it was thought that the whole picture might be due to metastatic melanotic sarcoma.

Third Operation—December 18 The lymph gland in the left groin was excised for diagnosis. Grossly, the glands were replaced by a black pigmented growth. The pathologist reported a metastatic melanotic sarcoma of the left inguinal gland.

Punctures were not made after the last operation, although nourishment and general nursing care was continued. The patient died after seven days.

December 25 Autopsy revealed metastases of the melanotic tumor to the left inguinal glands with extension into the femoral vein, retroperitoneal tissues, suprarenals, thyroid, thymus, brain, heart and bone marrow of the left femur.

EFFECT OF MERCUROCHROME-220 SOLUBLE ON THE GROWTH OF BACILLUS PYOCYANEUS*

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The work described in this article was undertaken following the observation in a neighboring hospital that *B. pyocyaneus* was found, in several contemporary cases, growing in dressings of mercurochrome-220 soluble after the first twenty-four hours' applications to a wound. The questions arising for solution concerned the unusual frequency of infections by *B. pyocyaneus*—*Pseudomonas aeruginosa* (Schueter)—usually an infrequent invader, and the specific value of mercurochrome as an antiseptic in infections with this microbe.

Pus was chosen as a medium for growth in an endeavor to imitate to some degree the conditions in the body, especially in infected surgical incisions. The pus used was sterile, having been drawn from a shoulder bursitis and having failed to produce any growth on blood agar plates or in dextrose broth. It was thick and creamy and on microscopic examination showed countless pus cells and ropey, mucus-like shreds, but no bacteria.

The cultures of *B. pyocyaneus* and *Staphylococcus aureus* used were fresh twenty-four-hour growths from plain agar slants. The characteristic coloring of *B. pyocyaneus* when grown in air made the readings extremely easy and definite.

The mercurochrome was the standard 2 per cent solution obtained from a freshly prepared stock supply on one of the surgical wards here. The iodine was the standard tincture of iodine.

EXPERIMENTS

The following experiments were performed:

Experiment 1—Tube 1, containing 2 cc of sterile pus, was inoculated with one loop of culture of *Bacillus pyocyaneus*, well mixed. Then 2 cc of a 2 per cent solution of mercurochrome was added as a separate layer without mixing, and the tube was placed at 37 C.

After twenty-four hours, one loop of pus from tube 1 was transferred to agar slant, tube 1 a, and this was incubated along with the original tube 1.

After another twenty-four hours, tube 1 a showed confluent growth of *B. pyocyaneus*, apparently equal to that in control tube 2 a below. Tube 1 a was then discarded. In tube 1 the mercurochrome was then thoroughly mixed with the pus, and this tube was continued at 37 C.

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On the next day, one loop of the mixed material from this tube 1 was transferred to agar slant, tube 1 *b*, which showed a moderately heavy growth of the organism in another twenty-four hours.

In this experiment, therefore, the bacillus of green pus grew in pus while the latter was exposed to an equal volume of 2 per cent mercurochrome in a layer over it for forty-eight hours and survived during subsequent exposure for twenty-four hours in the pus mixed with this equal volume of 2 per cent mercurochrome.

Experiment 2—Tube 2 containing 2 cc of sterile pus was inoculated with one loop of culture of *B. pyocyaneus*, well mixed and incubated at 37 C.

After twenty-four hours, one loop of pus from tube 2 was transferred to agar slant, tube 2 *a*, which was then incubated. Two cubic centimeters of mercurochrome was placed over the pus in tube 2, without mixing and tube 2 was then reincubated.

On the third day, tube 2 *a* showed a confluent growth of *B. pyocyaneus*. This was a control on tube 1 *a*. Mercurochrome was then run in tube 2 *a*, covering the growth completely. At the same time the mercurochrome in tube 2 was well mixed with the pus.

On the fourth day, the mercurochrome was poured off tube 2 *a*, and a loopful of the growth, which had been covered with the antiseptic for twenty-four hours, was transplanted to a fresh slant, 2 *a*₁, which was then incubated. Tube 2 *a* was reincubated after the surface of the slant had been rinsed once with distilled water. A loop of pus from tube 2, which had been mixed well with mercurochrome for twenty-four hours, was transplanted to an agar slant 2 *b*.

On the fifth day, tube 2 *a*₁ showed a confluent and moderate growth. Tube 2 *a* did not show a regrowth, no fresh colonies were found. Tube 2 *b* showed a slightly heavier growth than 1 *b* (experiment 1).

In this experiment, which acted as a control for the growth in experiment 1, the *B. pyocyaneus* was allowed to grow free from the presence of mercurochrome for twenty-four hours. The later addition and mixing of mercurochrome as in experiment 1 did not prevent the survival of *B. pyocyaneus*.

Furthermore, the covering of a growth of this organism on an agar slant with mercurochrome for twenty-four hours failed to prevent successful and free transplantation to another tube with subsequent good growth. This experiment was performed with *B. pyocyaneus* from three sources with identical results. The failure of growth on slant 2 *a* after mercurochrome was poured off was evidently due to exhaustion of the medium and to accumulated products of bacterial growth in the medium.

Experiment 3—Tube 4, containing 2 cc of sterile pus, was inoculated with one loopful of a culture of *B. pyocyaneus*, well mixed. Two cubic centimeters of tincture of iodine was then added as a separate layer without mixing, and the tube was incubated at 37 C.

The second day, a loopful of pus was taken from the bottom tube 4 and planted on an agar slant 4-*a*, which was incubated. The iodine was then mixed thoroughly throughout the pus in tube 4, and that tube was reincubated. On the third day tube 4-*a* showed no growth. It was reincubated. A loop of pus was transplanted from tube 4 to agar slant 4-*b* which was incubated. On the fourth day neither tube 4-*a* nor tube 4-*b* showed growth. Because of the possibility of unsuccessful transplantation of *B. pyocyaneus* in the first step the experiment was repeated a second and a third time with precisely the same results.

This experiment shows, therefore that *B. pyocyaneus* did not survive in the presence of the standard tincture of iodine when added either as a layer on the surface of the pus or mixed throughout.

Experiment 4—Tube B, containing 2 cc of sterile pus, was inoculated with a loopful of a culture of *Staphylococcus aureus* and incubated at 37 C

The second day, a loop was transplanted from tube B to agar slant B-a which was then incubated Two cubic centimeters of mercurochrome was added to tube B and mixed well Tube B was reincubated

On the third day, slant B-a showed a profuse growth of *Staphylococcus aureus* This was a control tube A loop was transplanted from tube B to agar slant B-b, which was then incubated

On the fourth day, tube B-b showed no growth This experiment showed that mercurochrome prevented the survival of *Staphylococcus aureus* when it was mixed throughout a medium of pus for twenty-four hours

Experiment 5—Tube C, containing 2 cc of sterile pus, was inoculated with a loopful of a culture of *Staphylococcus aureus*, mixed well, and 2 cc of tincture of iodine was poured on the surface but not mixed It was then placed at 37 C

On the second day, a loopful of pus from the bottom of the tube was transplanted to agar slant C-a, which was incubated The iodine was then stirred to mix it well throughout the contents of tube C

On the third day, tube C-a showed a sparse growth, a few colonies of *Staphylococcus aureus* A loopful was transplanted from tube C to agar slant C-b, which was incubated

On the fourth day, tube C-b showed no growth

This experiment showed that *Staphylococcus aureus* may survive in pus after the addition of iodine carefully run on the surface of the pus, but that this organism did not survive for twenty-four hours after the mixing of the antiseptic throughout

Experiment 6—Tube X, containing 2 cc of 2 per cent mercurochrome, was inoculated with one loopful of a culture of *B. pyocyaneus* and incubated at 37 C After twenty-four hours, a loop of mercurochrome from tube X was transplanted to agar slant X-a, which was incubated Examination of slant X-a on the third and fourth days showed no growth

This experiment showed that *B. pyocyaneus* did not survive in the pure solution of mercurochrome

Experiment 7—Tube Y, containing 2 cc of tincture of iodine, was inoculated with one loopful of culture of *B. pyocyaneus* and placed at 37 C On the second day, a loop of the iodine from tube Y was transplanted to agar slant Y-a, which was incubated Examination of slant Y-a on the third and fourth days showed no growth

This experiment showed that the *B. pyocyaneus* did not grow or survive in tincture of iodine

Both Young¹ and Todd² have reported the testing of solutions of mercurochrome against *B. pyocyaneus*, using emulsions of the living organisms Young's experiments showed this microbe to be somewhat more resistant to the antiseptic than were *B. coli* or *Staphylococcus*

1 Young, H H, White, E C, Hill, J H, and Davis, D M A Further Discussion of Germicides and Presentation of a New Germicide—Microxyl, Surg Gynec Obst 36 508 (May) 1923

2 Todd, A T Experimental and Clinical Investigations of Mercurochrome, Lancet 2 1017 (Nov 14) 1925

aureus Todd found that the bacilli of green pus were easily killed by mercurochrome if very few were present, but if larger amounts of the emulsion of organisms were added the bacilli survived. He attempted to explain this result on the basis of the presence of increased amount of bacterial protein.

In the present experiments the tests have been made under conditions more nearly simulating body environment, namely, in the presence of pus at body temperature, with exposure to the antiseptics over longer periods of time.

It is evident that mercurochrome has little, if any specific antiseptic action on *B. pyocyaneus* in pus, even when allowed full and complete access to the growth over twenty-four or even forty-eight hours.

Cultures of *B. pyocyaneus* have been isolated from the urine of three patients here within two months. Each of these specimens of urine showed large numbers of pus cells. The use of mercurochrome intravenously, as recommended for pyelitis by some physicians would appear ill-advised in such cases.

One might hazard a guess that the several concurrent infections of this organism, mentioned earlier in this paper, might be due to the fact that an antiseptic was being used which was of practically no value as a weapon against the bacillus of green pus. Such a situation gives rise to a false sense of security. The slightest defects in asepsis of technique might conceivably result in the carrying of the infection from one patient to another, which would have passed unnoticed in the presence of an effective antiseptic.

CONCLUSIONS

1. Mercurochrome is of little or no value as an antiseptic against *B. pyocyaneus*, in the presence of pus or other mediums suitable for its growth.

2. Mercurochrome has practically no effect on *B. pyocyaneus* in pus or on agar even when this organism is exposed freely to large quantities of the antiseptic for many hours.

3. Iodine will effectively destroy *B. pyocyaneus* under like experimental conditions.

4. Both mercurochrome and iodine destroy *Staphylococcus aureus* under like conditions.

5. *B. pyocyaneus* will not grow in pure solutions of mercurochrome or iodine without the presence of another medium.

A REVIEW OF UROLOGIC SURGERY

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(Concluded from page 828)

EXTERNAL GENITALIA

Meyer⁵² reviewed the work of replacing undescended testicles and reported a series of cases in which operation was performed by Torek's method. Many hypotheses have been advanced concerning the etiology of undescended and ectopic testicle, the most important of which concern the function of the chorda gubernaculi, the length of the spermatic vessels, the size of the inguinal canal, the size of the scrotum and the prenatal posture.

Histologic examination showed that spermatogenic cells are present and function in about 10 per cent of all cases. The interstitial cells, which have to do with the development of the secondary sexual characteristics, are always abundantly present. Such conditions are almost constant, and therefore the undescended testicles should always be saved.

Secondary complications occur. Malignant degeneration is not as common as is generally believed, and fear of it is not an indication for orchidectomy. Chronic inflammation, the presence of a potential or real concomitant hernia, practically always present, torsion of the spermatic cord and strangulation of the testicle are so frequent that surgical intervention is always indicated.

The best time to operate is before puberty, between the ages of 8 and 10 years if the undescended testicle is unilateral, and earlier if bilateral. The method described places the testicle where it is free from undue trauma, and gives it the best chance to develop, grow and function.

The usual incision in carrying out Torek's method of orchiopexy is like that in operation for hernia. The aponeurosis of the external

oblique is opened. The testicle, which lies in the inguinal canal, is freed and an incision made in the cremaster muscle parallel to the cord. The cord structures are separated out and the hernial sac is then isolated, ligated and resected. All fascial strands and adhesions are freed which allows the testicle to be brought down to a proper level. An oblique incision is then made in the thigh at about the region of the entrance of the long saphenous vein. A similar incision is made in the scrotum and the posterior lips of the two incisions are sutured. A hemostat is passed upward through the scrotum into the inguinal wound and the testicle grasped and brought down into the thigh-scrotum wound. The testicle is then sutured to the fascia lata and the anterior portion of the thigh-scrotum wound closed. The hernia is then repaired. The second stage of the operation is performed from four to six months after the first, the scrotum is separated from its attachment to the thigh and the testicle dissected from the fascia lata. The skin of the scrotum is then closed over the testicle.

Sixty-four operations were performed on forty-nine patients by Torek's method. Fifteen patients had bilateral, and thirty-four unilateral, undescended testicles. Results were traced in thirty-five cases and in all the testicles were satisfactorily situated in the bottom of a well formed scrotal sac. In no instance had the testicle atrophied or retracted against the pubic bone or come to lie in the upper portion of the scrotum. In the nine bilateral operations, the results were as good as in the unilateral. Three patients who had bilateral undescended testicles have married since operation and have led perfectly normal sexual lives. Two of the patients have not had children, but the third had a normal child eight years after marriage. Thirty-one operations were performed on patients before or at puberty, and thirty-three were performed after puberty. Of the operations performed on patients after puberty, Meyer has been able to follow the result in thirteen. The results have all been as satisfactory as in operations before puberty.

Thomas and Birdsall,⁵³ supplementing their previous work on the relative merits of vasopuncture and vasotomy, reported experimental studies. Vasotomy was performed twenty times on ten dogs and vasopuncture twenty times on another group of ten dogs. In eighteen of the first series the vas operated on was occluded in 55 per cent and both vasa were occluded in 33 per cent. In the series of twenty vasopunctures there was only one occlusion (5 per cent of the vasa operated on). Colloidal silver in a strength of 5 or 10 per cent is a safe antiseptic to use in the vas, providing there is no extravasation.

⁵³ Thomas, B. A. and Birdsall, J. C. Vaso-Puncture Versus Vasotomy Relative to Stricture Formation. An Experimental Study on Dogs. *J. Urol.* **16**: 529, 1926.

into the spermatic cord. Vasotomy, employing colloidal silver in a strength of 5 or 10 per cent, should be performed with great caution, as traumatism to the vas, and subsequent regurgitation and infiltration of the drug into the spermatic cord causes occlusion in over 50 per cent of operations.

Luy's⁵⁴ stated that the seminal vesicles may be washed either urethroscopically or surgically. Washing the vesicles through the ejaculatory duct is difficult. The surgical technic is as follows: A cutaneous incision is made at the root of the scrotum about 3 cm. long, the fat is then separated and the cord is lifted, the vas deferens is well isolated from its surrounding connective tissue for a distance of from 1 to 2 cm., a fine cannula is introduced into the canal, about 10 to 15 cc. of 5 per cent colloidal silver is injected. The wound is closed round a small drain. The patient should stay in bed for at least a week, on a light diet, and remain quiet for at least four days, since the colloidal silver remains in the seminal vesicles for this length of time. Luy's claims that his results have been good.

Hepburn⁵⁵ described an ingenious treatment for prolapse of the urethra in women. A median line suprapubic incision is made and the neck of the bladder is freed by blunt dissection. The urethra becomes prolapsed because of the poor attachment of the neck of the bladder to surrounding structures. When the finger is run down in the prevesical space, the neck of the bladder separates down to the urethra with little resistance or bleeding.

The hernia or prolapse of the urethra is reduced by traction on a suture in the dome of the bladder. In this drawn-up position, the anterior wall of the bladder is sutured to the structures in front of it, usually to the periosteum of the pubic bone and the posterior fascia of the rectus muscle. The legs must be apart so that an assistant can report when the prolapse is reduced, and whether it stays reduced after the stitches are placed. A rubber tissue drain is inserted to the prevesical space, and the wound is closed around it.

Verriotis and Defrise⁵⁶ stated that there is no definite basis for attributing the formation of congenital diverticulum of the female urethra to remnants of the wolffian body or from embryonic proliferation of the urethral wall. They classify these conditions as follows: (1) urethrocele, due perhaps to weakly developed portions of the urethral wall, especially in old age, or to extra-urethral trauma such as

54 Luy's, Georges. *Technique de lavage des vesicules seminales*, Paris chirurg 18 207, 1926.

55 Hepburn, T. N. *Prolapse of the Urethra in Female Children*, Surg Gynec Obst 44 400, 1927.

56 Verriotis, T., and Defrise, A. *Des diverticules uretraux chez la femme*, J d'urolog med et chir 21 97, 1926.

injuries at birth, or endo-urethral trauma such as the passage of a calculus, introduction of foreign bodies or attempts at catheterization (2) urinary pockets caused by inflammatory processes in the peri-urethral glands, and (3) cysts in the urethrovaginal septum. The symptoms are frequency, dysuria and dribbling. Diagnosis is made by noting the bulging of the vaginal wall, varying in size from 1 to 5 cm in diameter. Palpation reveals a soft tumor which on pressure empties into the urethra. Occasionally there may be slight incrustation. For further examination, probing, urethroscopy and roentgen ray may be used. A case is cited of a primipara aged 35, who six months after difficult delivery manifested the signs and symptoms mentioned. Urethroscopy and roentgenograms revealed an "egg-sized" diverticulum, its orifices 2 cm from the meatus. The diverticulum was excised, the patient recovered.

[ED NOTE—Bumpus gives the following classification of urethral diverticula]

A Congenital diverticula

B Acquired diverticula

(1) From dilatation of urethra from

(a) Calculus

(b) Stricture

(2) With perforation of urethra from

(a) Injuries to the urethra

(b) Rupture of abscesses into the urethra

(c) Rupture of cysts into the urethra

In the male, diverticula of the posterior urethra are generally of the acquired type. Bumpus states that the most frequent etiologic factor is a previous perineal operation. Since urethral diverticula may be associated with a normal bladder they may be easily overlooked unless the posterior urethra is carefully examined.]

Glockler and Rovinskij⁵⁷ cited a case of urethral fibrosarcoma in a baby girl, aged 13 months. Other complications made it impossible to operate on the tumor. Necropsy did not reveal metastasis. There were no adhesions or infiltration to the adjacent tissue. These facts suggested that operation, if attempted, might have been successful. Macroscopically, the tumor was a fibrosarcoma. The authors stated that they have not been able to find a similar case described in the literature at such an early age.

[ED NOTE—Fibrous tumors of the urethra are rare at any age, especially in infancy. Benign fibromas or fibromyomas occur more often in the female urethra than in the male. In the female they may be attached to any part of the urethra but usually to the posterior half.]

⁵⁷ Glockler, N. E., and Rovinskij, W. P. Ein Fall von Fibrosarcom der Urethra bei einem 13 monatigen Mädchen, abstr. Ztschr. f. urol. Chir. 20:4, 1926.

They are generally covered with urethral mucosa, are small and cause few symptoms. The benign tumors may grow rapidly and become very large. If they are large they are usually attached to the urethra by a pedicle, they are not attached to the periurethral tissues and shell out readily at operation. Malignant fibroma usually spreads rapidly and involves the surrounding tissues to such an extent that it may be impossible to determine its original site.]

Besley⁵⁸ reported a simple operation for traumatic rupture of the urethra in the male. A sound is passed down to the lacerated portion of the urethra, and longitudinal incision is made in the median line of the perineum, passing through skin and fascia until the bare end of the sound is well exposed, and the lacerated portion of the urethra can be seen.

After a free incision is made which exposes the torn urethra, a large rubber drainage tube is sutured into the wound down to the lacerated urethra. This provides for the escape of urine. The wound is then loosely packed with gauze, this is removed the following day and is not renewed. Six patients have been treated by this method without complication and with rapid convalescence.

Russell⁵⁹ pointed out that dilatation, although the accepted procedure for urethral stricture, is inadequate and unsatisfactory. He further pointed out that the urethra possesses two special attributes which make it suitable for excision of strictures: the capacity for spontaneous restoration after it has been slit up, no matter to what extent, and the elasticity or extensibility, which is physiologically controlled, and which enables the urethra to lengthen and shorten in response to changing conditions of the generative organs. This capacity for repair is described as follows:

The urethra when slit up is converted from a tube lined with mucous membrane into a "riband" covered with mucous membrane, its restoration is to be left entirely to natural processes, and will depend upon the obvious fact that a strip of mucous membrane flanked on either side by raw tissues, which tend naturally to fall together and cohere, will, when this has taken place, be of necessity converted into a tube.

Russell described an operation for excision of strictures which for several years has proved successful in his hands. The steps of the operation with the patient in the extreme lithotomy position, are as follows:

1. The angular incision is made, the apex being over the central point of the perineum. The deep fascia of the ischio-rectal fossa is opened on both sides with

58 Besley, F. A. Operation for Traumatic Rupture of Urethra in the Male, *Surg. Gynec. Obst.* **44** 372, 1927.

59 Russell, R. H. The Radical Operation for Urethral Stricture, *Brit. J. Surg.* **14** 250, 1926.

1 A blunt instrument, the left thumb and forefinger are introduced so as to grasp the front portion of the external sphincter. This muscle is severed from its attachment to the bulbospongiosus muscle at the central point and pushed backward. (The new method now diverges from the old, in which the next step conserved the membranous urethra.)

2 The mesial perineal incision is made which exposes the bulb and several inches of the corpus spongiosum and urethra, but without yet opening the urethra. The inflammatory mass comprising the stricture is defined by dissecting it on either side so as to loosen it in its bed, thus making it easy to lift it en masse when the proper moment arrives.

3 A full-sized straight metal bougie is passed down to the face of the stricture, clearly the whole of the urethra now occupied by the bougie is in good order and must be preserved. A transverse cut into the urethra over the point of the bougie is made, the bougie withdrawn and the transverse cut continued until the urethra is entirely severed (in all its coats) immediately in front of the stricture. The sound urethra is entirely detached from the inflammatory mass. During this step some slitting of the sound urethra may be done if the surgeon desires.

4 The inflammatory mass is dissected out of its bed on the triangular ligament from before backward and laterally. As it becomes loosened it is turned over backward so that the dorsal aspect of it with the urethra, the urethral foramen in the triangular ligament and the face of the triangular ligament itself, all come into view. The most distal portion of the mass, where the stricture must be, is now nearest to the surgeon. On the upper aspect of the mass the urethra will be seen emerging from its foramen in the triangular ligament to be more or less embedded on the surface of the mass for a little distance before it is plunged into the site of the stricture.

5 Removal of the stricture and the inflammatory mass with the minimal length of the urethra. The stricture must be situated at the distal end of the mass, and it must be between the distal end (previously called the face of the stricture when in situ) and the point at which the urethra is seen entering the mass on its dorsal surface. By a series of sections about 0.6 cm. thick, the distal end of the mass is cut away until the open mouth of the urethra appears, with perhaps a little urine flowing from it. A full-sized rubber catheter is passed through it into the bladder, thus proving that the stricture has been entirely removed. The remainder of the inflammatory mass is clipped away with knife and scissors, and perfectly sound proximal and distal urethras are brought together across an intervening gap that looks wide, but in reality is trivial in extent.

6 Both the proximal and (if not already done) the distal portion of the urethra are now freely slit up, so that the interior of the canal is displayed, being converted into a riband instead of a tube. The ends of the riband are sutured together with fine chromic catgut, the knots being on the mucous surface and eventually inside the urethra. In passing the sutures care must be taken to include a substantial share of the external coats of the urethra and corpus spongiosum. A good plan is to put one or two relaxation sutures in the outer coats. A rubber catheter is passed into the bladder and fastened with a suture to the skin, one catgut stitch passes through the skin on both sides at the level of the central point of the perineum, and takes up also the anterior end of the triangular flap, thus bringing it into its proper position. A suitable dressing is applied.

When the patient is returned to bed, a rubber tube is attached to the catheter, and the urine is conducted to a bottle suspended from the side of the bed. Each morning when the dressing is changed the bladder and catheter are gently washed through with boracic acid solution. The catheter is removed on the fifth day, and complete healing of the perineal wound rapidly takes place. Frequently the urine passes almost entirely through the penis during the first twenty-four hours after removal of the catheter.

Duvergey and Dax⁶⁰ reported hematuria in six cases of stricture of the urethra. In none was a general cause found for the loss of blood, and it was decided that the condition was entirely local. The authors stated that the urethra itself could not give rise to such severe hematuria. Operative and cystoscopic control proved that the bleeding came from above the urethra.

Two conditions are essential to the production of hemorrhage in cases of stricture of the urethra: congestion and infection. The diagnosis of the origin of such hematuria is important because if it is determined that it is due to the urethral stricture a good prognosis may be given, as the bleeding always disappears with the removal of the urethral obstruction. The treatment consists merely in dilating the stricture and reducing the infection of the bladder by lavage.

Demel⁶¹ described a case of varix formation in the anterior urethra of a boy, aged 14 years. Urethral bleeding was noticed following injury. Repetition of hemorrhage occurred at night and spontaneous bleeding might be seen at any time; the first urine passed was never tinged with blood. Cystoscopic examination was negative. Endoscopy revealed a papillary growth with a smooth surface in the anterior portion of the urethra, 8 cm. from the meatus. This was destroyed with the galvanocautery. A review of the literature revealed six similar cases with the site of the tumor similar to that in his case. Treatment may be carried out with galvanocautery, electrolysis, epinephrine or radium.

[ED. NOTE.—These small growths that bleed so freely are not infrequently angiomatous in type. Only a few cases are reported and undoubtedly, as Rokitsansky believes, are more representative of simple hypertrophy of vascular segments than of neoplastic overgrowth. They cause little pain or urinary discomfort, and in most cases respond readily to fulguration.]

Polyps and papillomas of the urethra are often seen. The majority are minute and are usually the result of long-standing urethral infection. They have little clinical significance. In most cases they disappear

⁶⁰ Duvergey, J., and Dax, L. *Les grandes hématuries chez les rétrécis*, *Presse méd* **35** 273, 1927.

⁶¹ Demel, Rudolf. *Zur Kasuistik einer seltenen Ursache von Harnrohrenblutung*, *Ztschr. f. Urol* **20** 125, 1926.

following treatment of the underlying infectious condition. In the male urethra, the small growths usually occur in the region of the verumontanum and the internal sphincter. Both the small and the large tumors respond readily to fulguration or snaring. Those which occur in the posterior urethra of the male may be pedunculated and occasionally interfere with the closure of the internal sphincter, those which occur near the external orifice are generally flat and sessile. Multiple and extensive growths are occasionally seen.]

McCarthy, Ritter and Klemperer⁶² undertook an extensive study of the verumontanum with special reference to the ejaculatory ducts. Their aim was to answer two questions: 1. What is the precise course taken by the ejaculatory ducts through the verumontanum and prostate? 2. Does an edematous or infiltrative closure of the lumen of the duct exist in a considerable number of cases?

Eighty specimens were studied, twenty were studied histologically. The ejaculatory ducts make a sharp dip through the verumontanum from the urethral orifice at an angle of approximately 45 degrees to the urethral floor. For the first millimeter and a half the ducts diverge and then converge for the next millimeter or two, until there is a thin septum of fibrous and elastic tissue separating them, this is easily penetrated, even though soft instruments are used. They then run parallel to each other and usually at a less acute angle through the prostate gland ending at the termination of, or within, the substance of this gland. At their division into the ampulla of the vas deferens and the duct of the seminal vesicles they are further away from the urethral floor.

The lumen of the duct of the seminal vesicle is 4.5 mm. in circumference, whereas the lumen of the ampulla of the vas deferens has a circumference of 3.1 mm., the circumference of the ejaculatory duct is noted at its termination, these measurements may be somewhat confusing. The similarity in size of the lumen of the ejaculatory duct with that of the duct of the seminal vesicle is accounted for by the fact that the ampulla opens on the mesial superior aspect of the ejaculatory duct.

The authors conclude as follows:

We feel that an explanation of the physiological fact that the seminal vesicles are distended when solutions are injected either through the vas deferens or ejaculatory duct is of utmost interest and importance.

1. The seminal vesicles are distended when fluids are injected through the vas deferens because:

(a) The normal resistance of the walls of the ejaculatory duct, which lumina become gradually smaller as they approach the urethral floor, causes the liquids to flow toward the seminal vesicles.

⁶² McCarthy, J. F., Ritter, J. S., and Klemperer, Paul. Anatomical and Histological Study of the Verumontanum with Special Reference to the Ejaculatory Ducts, *J. Urol.* **17** 1, 1927.

(b) A large muscular organ (the prostate) surrounds the ejaculatory duct and offers resistance to their distention

(c) The ejaculatory duct has no musculature of its own to overcome the resistance of the prostatic musculature

(d) The lateral wall of the duct of the seminal vesicle contains elastic tissue which is less resistant to distention than muscle tissue

2 The seminal vesicles are distended when solutions are injected by way of the ejaculatory duct prior to any solution appearing in the vas deferens because

(a) The duct of the seminal vesicle is a direct continuation of the ejaculatory duct

(b) The lateral wall of the duct of the seminal vesicle contains elastic tissue and is therefore less resistant and more readily distended than the ampulla of the vas deferens

(c) The lumen of the ampulla of the vas is surrounded by thick muscle walls and its orifice opens supero-mesially into the ejaculatory duct

(d) The lumen of the ampulla contains several valve-like protecting folds within its lumen which tend to obstruct the entrance of any fluid into the vas deferens

Redi⁶³ reported a case of rupture of the penis following trauma. Applications of ice and immobilization in cardboard tubes effected cure in a few weeks. There were no sequelae. The points of resistance of the distended organ, albuginée propre, fascia of the penis and traverses lamelliformes, being reduced to extreme thinness, are likely to break under the influence of obliquely acting forces. The symptoms are pain, deformity, swelling and extravasation of blood. The fracture is easily distinguished from contusion, on careful palpation. The prognosis must be reserved on account of possible complications, suppurative hematoma, gangrene in case of intact urethra and anuria, infiltration of urine and phlegmon, in cases in which the urethra is torn. The scarring itself may also bring about the formation of pseudarthrosis, in certain cases rendering coition impossible.

There are two methods of treatment. (1) the surgical method to which certain surgeons resort in every case and which consists in a large opening of the hematoma and suture of the corpus cavernosum and fascia with immobilization, this method is effective, but should be used only in cases in which the hematoma is extensive and offers little hope of spontaneous resorption, (2) if the hematoma is circumscribed, application of ice, immobilization and carefully performed catheterizations will often bring about cure, if the urethra is ruptured, the prognosis is more serious, a permanent catheter will be necessary, and if this is unbearable to the patient, external urethrotomy with a plastic reconstruction of the penis is necessary.

⁶³ Redi, Rodolfo. Un cas de fracture du penis, *J. d'urolog. med. et chir.* 22 36, 1926.

ble at any age, by the use of modern instruments, and that such examination should always be made. As cystoscopy in young children must be done under general anesthesia, it is most important to complete every other phase of the examination before it is undertaken. If cystoscopy is carried out it should be complete in every detail, including divided specimens of urine for bacteriologic, chemical and microscopic examination, inoculation of animals, phenolsulphonphthalein and other functional tests, together with roentgen-ray examination and pyelography when these are indicated. Rarely does severe reaction follow cystoscopy and ureteral catheterization in these very young subjects, it is much less frequent than in adults. Renal tuberculosis is much commoner in children than is ordinarily believed, and may be accompanied by secondary infection.

Nonoperative treatment should be the rule whenever possible, operation being resorted to only in cases of dire emergency in children under the age of 4 years. Operative repair of congenital lesions, such as hypospadias, epispadias and undescended testicle with its accompanying hernia, should be performed only after the child has reached the age of 4. Congenital malformations causing obstruction to proper urinary drainage of any part of the urinary tract should be relieved as soon as it is discovered.

Beer⁶⁷ pointed out some analogies between the urinary and biliary tracts. In comparing cholesteremia and uricemia he showed that cholesterol is a more or less specific hepatic excretion, while uric acid bears a somewhat similar relation to renal function. By experimental feeding, both substances can be increased in the blood and in the urine. In certain conditions, such as the postinfective period in typhoid fever, the blood cholesterol is increased, while in other conditions, such as the crisis in pneumonia, the uric acid content of the blood is increased. In bilateral renal obstruction, the uric acid is the first component to be increased in the blood. In choledochus obstruction, one of the first signs is accumulation of cholesterol in the blood.

In regard to lithiasis striking analogies are discerned. The stasis or primary cholesterol stones are compared with uratic calculi which are presumed to be performed without the agency of gross infection from "a temporary spilling over of the stone material, or an increased excretion which may contribute to produce the colloidal instability that leads to the precipitation of the stones." When infection sets in a totally different type of stone occurs. In the biliary tract, the cholesterol-pigment calcium stones are found, and in the urinary tract, the phosphate stones.

⁶⁷ Beer, Edwin. Analogies Between the Biliary Tract and the Urinary Tract, *Ann Surg* 84: 517, 1926.

In regard to infection, it is striking to see how readily the bacteria are passed through these glands without apparent injury to the parenchyma. This transit through the two systems seems to leave no permanent injury unless foreign bodies or obstructive conditions obtain, and then local inflammatory changes may be induced. A comparison of the bacillary and coccic infections of the kidney and liver is made. Beer quotes Naunyn, Aschoff and others as believing that acute hepatitis, somewhat analogous to acute pyelonephritis, may be frequent, and he feels that some of the changes of the cholelithotic liver are developed in some way analogous to the repeated infections of the renal parenchyma which lead to the peculiar scarred kidney in long standing cases of pyelonephritis.

[ED NOTE—It is interesting to consider Beer's comparisons of these two great systems. It has been shown experimentally that increased excretion of oxalates from the kidneys may produce lithiasis, and for many years Naunyn and his followers have held that hyperexcretion of cholesterol is responsible for the production of biliary calculi of the pure pigment type. Beer's observation that typical attacks of biliary and renal colic may occur without evidence of either stone or gross inflammation is timely, as many surgeons and urologists are puzzled by these occurrences, which are baffling from the standpoint of treatment.]

Jullien⁶⁸ observed that abdominal distention in the fetus is an extremely rare cause of dystocia. He cited a case in which, after delivery of the head, the body could not be delivered until the abdomen of the fetus was punctured and 3 liters of urine withdrawn. The cause of the retention was obliteration of the urethra. The remaining abdominal organs had been retarded in their development.

Lagemann⁶⁹ described a case of a malingerei with apparent chyluria. The patient, a man, aged 40, had milky urine following an attack of influenza. The temperature was 39 C and the patient appeared to be ill. The milky urine contained 14 per cent albumin and also casein. The phenomenon was noticed for twenty-two days, the appearance of the urine varying from milk-white to complete clarity. Following ureteral catheterization the turbidity disappeared. On the wall of the bladder were many membranous shreds, although the mucous membrane appeared entirely normal. It was finally concluded that the patient had secretly injected milk into his bladder.

68 Jullien, F. Dystocie grave par retention d'urine chez le fœtus, *Rev franç de gynec et d'obstet* **21** 24, 1926.

69 Lagemann, Clemens. Ein Fall von künstlich erzeugter Chylurie, *Arch f klin Chir* **139** 240, 1926.

Randall and Muschat⁷⁰ reported the results of their study on the hydrogen ion concentration of the various secretions of the urogenital tract

Acidification of the urine is an important problem in urologic surgery. Acidity is desirable from two points of view, but for one and the same purpose. Most secondary infections of the urinary tract are due to the colon bacillus. This organism suffers marked inhibition in growth when the reaction of the urine is markedly acid, at or below p_H 5.5. Rendering the urine acid and bringing it to p_H 5.5 is a good method of counteracting the invasion and growth of the colon bacillus. Many substances have been advocated and are in use for this purpose, those most frequently used being sodium benzoate, ammonium benzoate, acid sodium phosphate and ammonium chloride. They found that of these, ammonium chloride was more constant and stronger in its action than the others.

Their study of the influence of hydrogen ion concentration on the activity of the spermatozoa indicate that the reaction of the environment of the spermatozoa plays an important part in the physiologic mechanism involved in impregnation. The maintenance of a weak alkalinity in the genital tract in the female is of utmost importance, and cases of sterility should demand such study. The vaginal secretion is weakly acid, but the cervical secretion is almost neutral and it is assumed that the uterine secretion is probably weakly alkaline, meeting the vital requirements of the spermatozoa and probably stimulating them to great activity as they progress into this more favorable environment. Their work also shows that inflammatory conditions do not influence the reaction of the prostatic secretion, which remains as in the normal, that is, p_H 7.3, and, thus that such conditions do not play any part in changing the function of these secretions.

⁷⁰ Randall, Alexander, and Muschat, Maurice. Hydrogen-ion Studies on Various Secretions of the Uro-genital Apparatus, *J. Urol.* **16** 515, 1926.

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demarcation at the anterior axillary line. This area of density suggested an effusion in the left pleural cavity at that site.

At discharge the left side of his chest had cleared up almost entirely. There was no dulness in the back and no signs of fluid or of consolidation. The right side showed a decreasing pneumothorax with a moderate amount of fluid at the base. In a letter several weeks afterwards, the patient reported himself practically well.

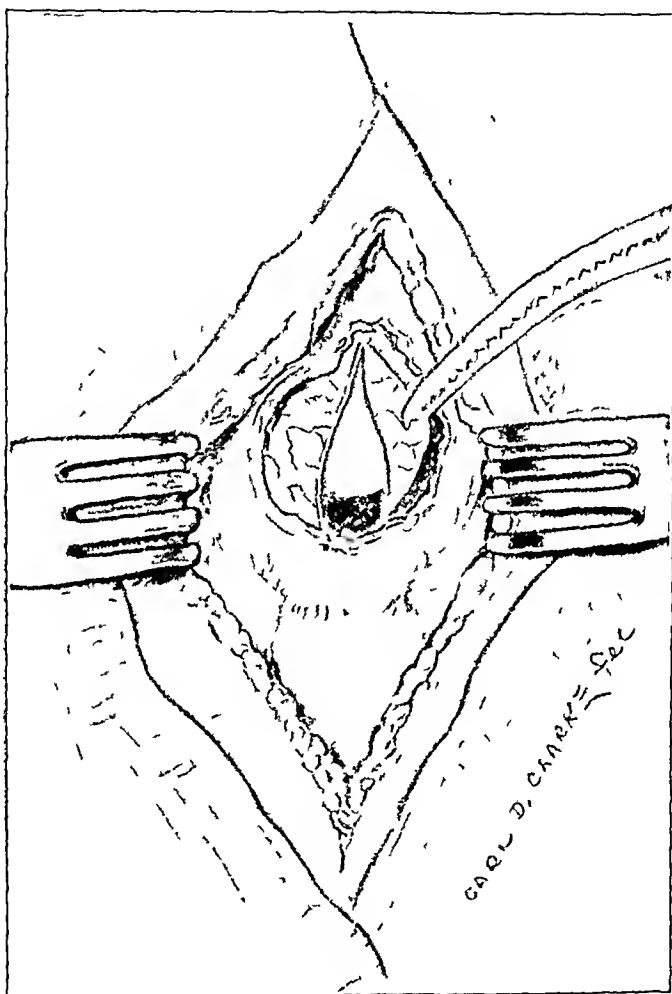


Fig 1—Transsternal pericardiotomy

COMMENT

The ten patients in this series were operated on for purulent effusion of the pericardium, with six, or 60 per cent cures, and four, or 40 per cent deaths. These figures correspond closely with the general mortality rate for all patients treated by incision and drainage. In the first four cases pericardiotomy was performed after the sternum had been trephined. The Hudson drill was used, and the opening was enlarged by rongeur forceps. The opening was made immediately above the junction of the second portion of the sternum with the ensiform

appendix. By using the rongeur forceps, the enlargement was made to the left of the midline. This method has a number of advantages. It can be done easily under local anesthesia and the internal mammary artery is not encountered.

The vent in the sternum comes down directly on a small triangular area which usually is not overlaid by the pleura, so that the pericardium is immediately exposed after the removal of a small amount of areolar tissue that generally lies in this space. The most serious disadvantage of this method of approach is that the firm unyielding walls of the opening in the sternum to some extent limit palpation of the pericardial sac by the examining finger although this is less true in children than in adults. Bexman (1891) is the only other operator to use this approach for draining pus from the pericardium. He went through the sternum, however at the level of the third costal cartilage. Bacon's experience at the autopsy table has impressed him with the comparative ease with which the pericardium may be explored through an opening in the sternum. He tabulates the advantages of this route, as follows:

- 1 It is anatomicallv correct
- 2 It affords an easy approach to the pericardium
- 3 It supplies the best possible drainage
- 4 It permits ready inspection of the heart and pericardial cavity
- 5 It is devoid of mechanical danger, such as hemorrhage and rupture of the pleura
- 6 It can be done under gas anesthesia
- 7 It requires only from five to fifteen minutes for its completion
- 8 It does not leave deformity
- 9 It offers the least possible chance of spreading infection to the pleural or to the peritoneal cavities

In the four cases of our series in which it was used, it proved fairly satisfactory, but it was discarded in the later operations for avenues giving greater access to the pericardium.

In cases 5, 6 and 7, an oblique incision was made in the skin, parallel to the costal margin, extending for about 10 cm. from the base of the ensiform process toward the left. The incision through the underlying structures hugged closely the under surface of the costal arch, and with rongeur forceps about 5 cm. of the left fifth, sixth and seventh costal cartilages were removed. This approach exposes the mammary vessels, but no difficulty was experienced in ligating them and thus controlling bleeding from them. The margin of the left pleura invariably came into view, but this was easily pushed aside, and the pericardium was exposed. The pericardium was grasped with the forceps and incised. This route places the incision in the pericardium near its base, allows palpation of the left side of the pericardial sac and makes placing of the drains somewhat easier than in the approach through the sternum.